


Ocular Disease Clinical Potpourri  
Something New, Something Old, Something to Make Us All  
Better Clinicians, and Something to Make Say Hmmm!


Greg Caldwell, OD, FAAO  
Sunday, April 24, 2022  
Annual Nutrition and the Eye Symposium



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Nutrition and Eye Care  
The Connection Between Function, Structure, and  
Molecular/Nutritional Changes


Greg Caldwell, OD, FAAO



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Disclosures- Greg Caldwell, OD, FAAO

- The content of this activity was prepared independently by me - Dr. Caldwell
- Lectured for: Alcon, Allergan, Aerie, BioTissue, Kala, Maculogix, Optovue, RVL, Heru
- Advisory Board: Allergan, Sun, Alcon, Maculogix, Dompe, Visus, Eyenovia
- Involve: PA Medical Director, Credential Committee
- Healthcare Registries – Chairman of Advisory Council for Diabetes
- I have no direct financial or proprietary interest in any companies, products or services mentioned in this presentation
- Disclosure: carotenoid Pharmedex scanner owner, Maculogix owner, Optovue OCT and OCT-A owner
- The content and format of this course is presented without commercial bias and does not claim superiority of any commercial product or service
- Optometric Education Consultants – Scottsdale, AZ, Orlando, FL, Mackinac Island, MI, Nashville, TN, and Quebec City, Canada - Owner



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Financial Obligations



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Thank You for This Opportunity



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My Practice

I am a clinician first then a scientist. Some are scientists first then clinician. I need to simplify for patient and patient care. Science is great but not good if there isn't a clinical application. Some lectures are science based without clinical application. My lecture will be a hybrid. Showing clinical applications of the science.



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### Patients Are Expecting

- ~ Wellness
- ~ Prevention
- ~ Early detection

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### Question?

- ~ Who in here would consider themselves as an integrative optometrist?
- ~ Who has done or recommended?
  - \* Supplements, vitamins, AREDS2
  - \* Omegas, EPA, DHA
  - \* Vital tears – ASED
  - \* Regener-Eyes
  - \* Amniotic membranes
  - \* CBD
  - \* Probiotics

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### Allopathic vs Integrative Medicine

- ~ "Allopathic medicine" is a term used for modern or mainstream medicine
  - \* Conventional medicine, mainstream medicine, biomedicine
  - \* Treating conditions and symptoms with its "opposite"
  - \* Health system in which medical doctors, nurses, pharmacists, and other healthcare professionals are licensed to practice and treat symptoms and diseases
  - \* Using medication, surgery, radiation, therapies, and procedures
- ~ Complementary and integrative medicine are commonly used along with mainstream medicine
  - \* Homeopathy, naturopathy, chiropractic care, Chinese medicine
- ~ Allopathic or modern medical schools have recently added more study and information on how food and nutrition can help prevent and treat disease
  - \* More education is being offered on integrative approaches and potential interactions with mainstream medicine

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### Medical Practices

- ~ Allopathic medicine
  - \* Western medicine
- ~ Alternative "homeopathic"
- ~ Functional
  - \* Medicine of why, treat the cause
- ~ Integrative medicine
  - \* Complementary medicine - Eastern complimenting Western

What is integrative medicine?

The practice of integrative medicine refers to the **blending of conventional and evidence-based natural and complementary medicines and/or therapies with lifestyle interventions to deliver holistic, patient-centred care.**

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### Endogenous and Exogenous Free Radical Formation

**Antioxidants**

**FORMATION OF FREE RADICALS**

*(Note: The diagram also includes chemical equations for aerobic respiration and irradiation.)*

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### Oh no

- ~ Increasing exogenous free radicals
- ~ Less antioxidant protection in our diet
- ~ More bad and less good

Is an orange of the 1950's equivalent to 21 of today's oranges?

An orange from the 1950's was full of vitamin A, precious for our sight and our immune defenses. To attain the same amounts today, you would have to consume 21 of them. Onions and potatoes no longer contain any trace of it. The iron content in meat? Divided by 2. Calcium in broccoli? Divided by 4. To ingest the vitamin C contained in an apple from yesteryear, you would have to eat 100 today.

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### Chronic and Low-Grade Inflammation

Science has proven that chronic, low-grade inflammation can turn into a silent killer that contributes to cardiovascular disease, cancer, type 2 diabetes, diabetic retinopathy, cataracts, macular degeneration, and many other conditions

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### Chronic and Low-Grade Inflammation

Like cancers and other slow-burn diseases, identifying these conditions early can make the difference between full recovery or a dramatically reduced quality of life or even death (vision loss or blindness)

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### “Choose Your Parents Wisely”

- ~ This just isn't as true as it's used to be
- ~ Lifetime health
  - \* 8% genetics “Picking your parents wisely”
    - DNA in our nucleus
      - Can't be influenced
  - \* 92% epigenetics
    - Lifestyle choices = we can influence
    - Turn on/off gene expression

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### Biomarker

- ~ Test that has meaning
- ~ Biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease.
- ~ A biomarker may be used to see how well the body responds to a treatment for a disease or condition
- ~ Blood pressure, heart rate, genetic testing, IOP

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### Predictive Biomarker

- ~ Used to identify individuals who are more likely to respond to exposure to a particular medical product or environmental agent
- ~ The response could be a symptomatic benefit, improved survival, or an adverse effect
- ~ A value that we can guide therapy around
  - \* HbA1c
  - \* C-Reactive Protein
  - \* Plasma Homocysteine
  - \* Vitamin D (25-HydroxyD)
  - \* Omega 3 index
  - \* Carotenoid

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### DNA Sciences

- ~ Genomics = all of our genes
- ~ Genetics = individual genes
- ~ Epigenetics – how our genes internal and external environments

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### Exposome

The exposome can be defined as the measure of all the exposures of an individual in a lifetime and how those exposures relate to health. An individual's exposome begins before birth and includes insults from environmental and occupational sources. Understanding how exposures from our environment, diet, lifestyle, etc.

<https://www.cdc.gov/niosh/topics>

Exposome and Exposomics - NIOSH Workplace Safety and Health Topic - CDC

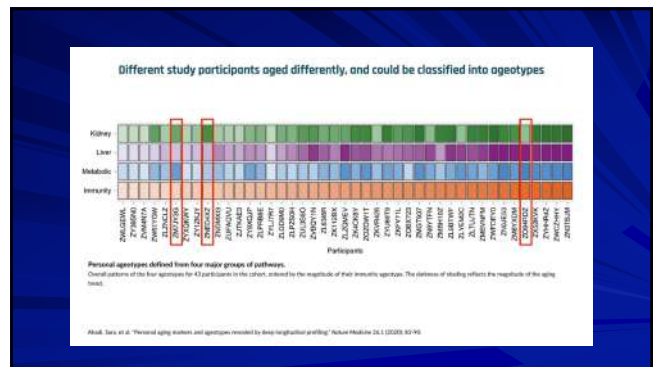
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### Key Tenants of Aging, Performance and Vitality

- Oxidative Stress / Inflammation
- Hormonal Balance
- Stress Hormones
- Glucose / Insulin Regulation
- GUT integrity and microbiome diversity
- Immune Balance
- Environmental Exposure/Burden
- Individuality

Credit to: James LaValle, RPh, CCN

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### OBJECTIVES

- Understand the overlapping processes that result in mitochondrial dysfunction and immunosenescence
- Discuss emerging diagnostic modalities to detect immune decline
- Learn to execute an effective nutraceutical and lifestyle program to correct mitochondrial and immune dysfunction

Credit to: Elroy Vojdani, MD – David Battersby, The Role of Mitochondrial Dysfunction in Immunological Decline: Emerging Diagnostic Tools and Nutraceutical Interventions

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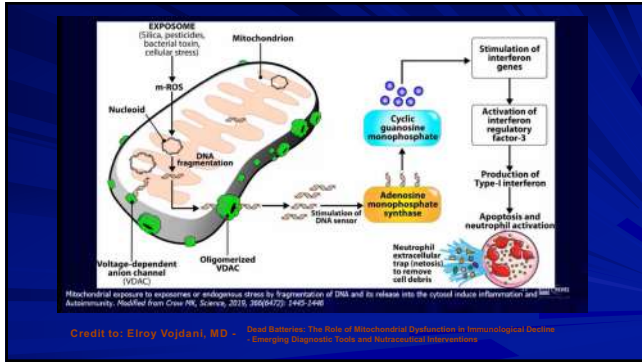
### Inflamm-aging

One of the consequences of failing mitochondria due to aging, beyond mtROS, is the release of mtDNA. Plasma levels of mtDNA increase gradually after the fifth decade of life, correlating with elevated levels of pro-inflammatory cytokines (i.e., TNF- $\alpha$ , IL-6, RANTES, and IL-1ra)

These data indicate that mtDNA may promote the production of pro-inflammatory cytokines in aging. Because cell stress, senescence and death are a part of the pathophysiology of aging designing new therapeutic strategies against circulating mtDNA, or other mtDAMPs, or their cognate receptors (e.g., TLRs or FFR1) may be a viable strategy to approaching IA and its associated conditions.

Credit to: Elroy Vojdani, MD – David Battersby, The Role of Mitochondrial Dysfunction in Immunological Decline: Emerging Diagnostic Tools and Nutraceutical Interventions

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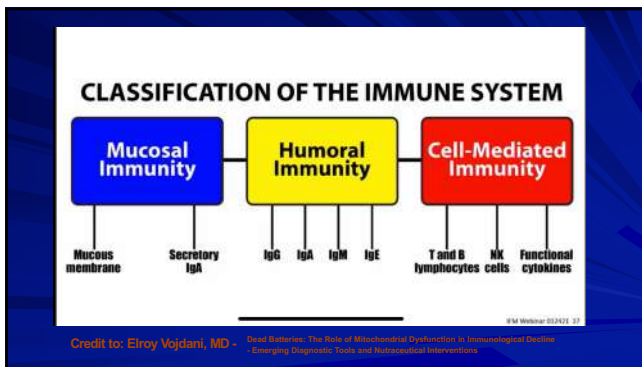
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### Fun Facts I Have Learned About the Mitochondria

- ~ Mitochondria produce energy from organic matter
- ~ They produce 90% of energy in the body
- ~ In return they produce 90% of the free radicals
- ~ When they become dysfunction when get many clinical consequences
- ~ Mitochondria are very sensitive to reactive oxygen and need antioxidant support
- ~ Mitochondria are one of cellular organelles
  - \* Electron transport chain – uses co-enzyme 10, and many other micronutrients
  - \* Brain cell has 1-2 million/single neuron
  - \* Heart cell has 5,000/cell
  - \* Liver cell has 1000-2000/cell
  - \* Photoreceptors 498/cell
  - \* RPE cells > 700/cell

The ellipsoid contains a densely-packed array of mostly elongated mitochondria arranged broadly parallel to the long axis of the photoreceptor. The cell contained **498 individual mitochondria**

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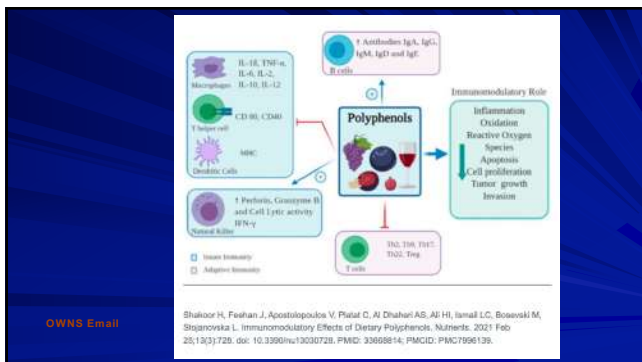
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### Completely Normal Immunotype

In the normal immunotype, the different cells involved in the immune system such as macrophages (Mφ), antigen-presenting cells (APC), T-helper cells, B cells and more all play together in concert to produce the most beautiful harmony called **immune homeostasis**.

**Credit to: Eroy Vojdani, MD - David Baharav, The Role of Mitochondrial Dysfunction in Immunological Diseases: Emerging Diagnostic Tools and Nutritional Interventions**

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### Dictionary

Definitions from Oxford Languages

Search for a word

**se-nes-cence**  
 /səˈnɛsəns/  
 noun **BIOLOGY**  
 the condition or process of deterioration with age.  
 • loss of a cell's power of division and growth.

**Google Search Definition**

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### Hallmarks of Immunosenescence

- Low CD4 and/or CD8 counts
- Low T Reg count
- TH1 dominance
- TH17 dominance
- Low NK Cell activity
- Low B cell counts
- Low/suboptimal total immunoglobulins
- Low Sec IgA levels
- Low antibody response to antigen presentation (vaccines)

© 2014 Wolters Kluwer | 43

Credit to: Eloy Vojdani, MD - David Baharwall, The Role of Mitochondrial Dysfunction in Immunological Decline: Emerging Diagnostic Tools and Nutritional Interventions

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Nature Immunology VOL 22 | June 2021 | 687-698

### Interventions that might improve T-cell aging

Hallmarks aging | 47

Credit to: Eloy Vojdani, MD - David Baharwall, The Role of Mitochondrial Dysfunction in Immunological Decline: Emerging Diagnostic Tools and Nutritional Interventions

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### Intervention

Boosters of mitochondria

Credit to: Eloy Vojdani, MD - David Baharwall, The Role of Mitochondrial Dysfunction in Immunological Decline: Emerging Diagnostic Tools and Nutritional Interventions

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### Intervention

- Resveratrol
- ECGG
- Curcumin
- Quercetin
- Fish Oil
- Probiotics
  - Lacto
  - Bifido

Credit to: Eloy Vojdani, MD - David Baharwall, The Role of Mitochondrial Dysfunction in Immunological Decline: Emerging Diagnostic Tools and Nutritional Interventions

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### Intervention

Boosters of mitochondria

Credit to: Eloy Vojdani, MD - David Baharwall, The Role of Mitochondrial Dysfunction in Immunological Decline: Emerging Diagnostic Tools and Nutritional Interventions

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Credit to: Eloy Vojdani, MD - David Baharwall, The Role of Mitochondrial Dysfunction in Immunological Decline: Emerging Diagnostic Tools and Nutritional Interventions

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**Take Home Points**

- Mitochondrial injury and immunological injury are synonymous
- Inflamm-aging, susceptibility to infection, and T cell aging are the hallmarks of this overlap
- Susceptibility to infection and T cell aging can be quantified with immunotype testing
- Treatment should include removal of ongoing chronic immune insult (inflammation) and immune rejuvenation
- Lifestyle Interventions:**
  - Anti-inflammatory diet
  - PRK
  - IF
  - TRP
  - Cold-hot therapy
  - Light therapy
  - Mitochondrial boosting nutraceuticals
  - EXERCISE

**Credit to: Etroy Vojdani, MD** - *Reset Balance: The Role of Mitochondrial Dysfunction in Immunological Decline: Emerging Diagnostic Tools and Nutritional Interventions*

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**Key Tenets of Aging, Performance and Vitality**

- Oxidative Stress / Inflammation
- Hormonal Balance
- Stress Hormones
- Glucose / Insulin Regulation
- GUT integrity and microbiome diversity
- Immune Balance
- Environmental Exposure/Burden
- Individuality

**Credit to: James LaVelle, RPh, CCN**

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**The Saudade Hormonal Symphony™**

**Credit to: Filomena Trindade, MD**

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**What Effects Thyroid Function: Production of Thyroid Hormones**

**Credit to: Filomena Trindade, MD**

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**Thyroid Function: Factors increasing conversion of T4 to T3**

**Credit to: Filomena Trindade, MD**

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**Thyroid Hormones: Factors improving cellular sensitivity to thyroid hormones**

**Credit to: Filomena Trindade, MD**

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**Thyroid Function: Inhibitors of Thyroid Hormone Production:**

- Pituitary**
  - Direct inhibition (trauma, radiation, medications)
  - Thyroiditis (autoimmune)
- Thyroid Gland**
  - Iodine deficiency
  - Autoimmune disease (Hashimoto's, Graves)
  - Selenium deficiency
  - Cystitis (thyroid)
  - Low iodine intake
  - High iodine diet
  - Elevated cortisol
  - Chronic stress
  - Decreased iodine in liver
- Cell Nucleus**

Credit to: Filomena Trindade, MD

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**Thyroid Function: Factors Decreasing conversion of T4 to T3**

- Pituitary**
- Thyroid Gland**
- T4**
- Cell Nucleus**

Factors: Stress, Trauma, Low-calorie diet, Inflammation (cytokines, etc.), Toxins, Infections, Liver/kidney dysfunction, Rx medications

Credit to: Filomena Trindade, MD

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**Two Major Pathways of Metabolism & Detoxification**

Phase I: Reactive Intermediate → Phase II: Elimination

Factors: Genotoxins, Oxidative Stress, Phase II enzymes

Credit to: Filomena Trindade, MD

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**Key Tenants of Aging, Performance and Vitality**

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Credit to: James LaValle, RPh, CCN

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**Electron Microscopy of GUT Epithelial Barrier Healthy vs. Non-Healthy**

Healthy: Commensal bacteria, Tight junctions

Non-Healthy: Opportunistic pathogens, Gaps in barrier

Credit to: James LaValle, RPh, CCN

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**Key Tenants of Aging, Performance and Vitality**

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- Individuality

Credit to: James LaValle, RPh, CCN

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### Metaflammation

- Also known as "Inflammaging" and metabolism induced inflammation
- Chronic low-grade inflammatory sequelae
- Increases aging processes and metabolic signaling issues
- Caused by AND leads to "diabesity":
  - Insulin resistance; type 2 diabetes
  - Obesity
  - Stress
  - Diet
  - LPS induced
  - Liver / kidney issues

Friedlander, J. et al. Inflammaging and metabolic syndrome: mechanisms and implications for clinical practice. *Diabetes Care*. 2020;43(1):1-11

Credit to: James LaVelle, RPh, CCN

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### Metaflammation Constructs

Credit to: James LaVelle, RPh, CCN

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### Metaflammation Induces Catabolic State

Stimuli	Inflammation	Effect	Switch off inflammation	Healing
<ul style="list-style-type: none"> <li>• Damaged cell debris</li> <li>• Irritant chemicals</li> <li>• Pathogens</li> <li>• Intrinsic cell defect</li> </ul>	Attempts to remove damaged cell debris, irritants, or pathogens	Eliminates the cause of inflammation		
Systemic effects				
<b>Sarcopenia</b> ↓ Dynamic muscle perfusion ↓ IGF1 production and signalling	<b>Anaemia</b> ↑ Hepcidin ↓ Ferritin ↓ Iron absorption and recycling ↓ EPO production and signalling	<b>Insulin resistance</b> ↑ TNF-R1 ↑ TLR4 ↑ JAK ↑ IRS1 and IRS2 activation ↓ Insulin signalling	<b>Osteoporosis</b> ↑ TNF, IL-1β, IL-6, and RANKL ↓ Osteoclasts ↓ Osteocalcin	<b>Others?</b> Neurogenesis ↓ Neurogenic growth factors ↓ Neurogenesis ↓ Cell plasticity Mitochondrial function and biogenesis ↑ TNF, IL-1β, and IL-6 ↓ Respiration and ATP synthesis ↓ NAD <sup>+</sup> :NADH ratio ↓ PGC1α

Hernandez, L. et al. Inflammaging, chronic inflammation in aging, cardiovascular disease and frailty. *Nat Rev Cardiol*. 2019;15(12):742-757

Credit to: James LaVelle, RPh, CCN

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Google Search Definition

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### Newer Documented Benefits

## Going beyond the generalizations of "antioxidants"

- Internal network of antioxidants
  - Vitamin E (food sources: wheat germ, seed oils, nuts, seeds, greens)
  - Vitamin C (food sources: citrus fruits, cherries, berries, papaya, broccoli, kiwi)
  - Polyphenols (e.g., teas, fruits such as apples and berries, vegetables)
  - Carotenoids (e.g., sweet potato, bell peppers, yam, carrots, tomatoes)
- Internal system of antioxidant defense enzymes
  - Superoxide dismutase (SOD)
  - Catalase
  - Glutathione peroxidase
- External intake of antioxidants
  - Be aware of double-edged nature with high amounts of isolated agents as they can act as pro-oxidants

Walle, M., Maki, A., Degen, G., et al. Strengthening the Immune System and Reducing Inflammation and Oxidative Stress Through Diet and Nutrition. *Comprehensive Reviews in Food Safety and Nutrition*. 2021;15(1):1-15

Dexanna Minich, MS, PhD, FACN, CNS

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### Assessing Phytochemical Intake

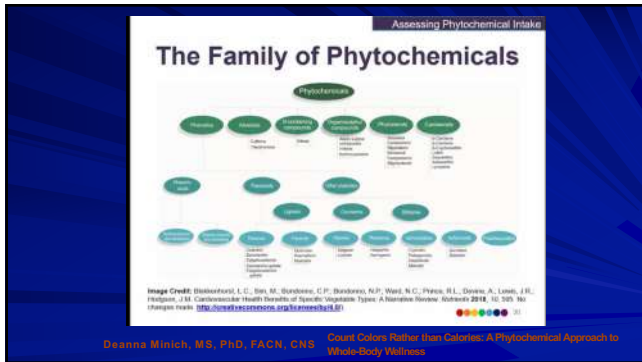
## The 'phytonutrient gap'

- 69% fall short in green
- 78% fall short in red
- 86% fall short in white
- 88% fall short in purple/blue
- 79% fall short in yellow/orange

American Phytochemical Society. *Nutrition Health Institute*. 2016. <https://www.americanphytochemicalsociety.org/Portals/0/PhytochemicalIntakeReport.pdf>

Dexanna Minich, MS, PhD, FACN, CNS

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- ### 3 Types of Products in the Market
- Full Spectrum CBD
    - Contains trace amounts of THC (delta 9 THC)
    - Should include other cannabinoid compounds
    - Multiple cannabinoids and terpenes
    - Lower dose than isolate by 5-10 times
    - Stable shelf life
    - Might fail a work or drug recovery program drug test – avoid
  - Broad Spectrum CBD
    - No detectable THC
    - Other phytocannabinoids, terpenes
    - Won't fail a drug test
  - Isolate CBD
    - Only CBD
    - Least medical benefits
    - Won't fail a drug test
    - Need high doses – 5-10 times more than full spectrum
    - Unstable shelf life
- Doesn't work for everyone and everything  
 But CBD has a broad spectrum of uses*

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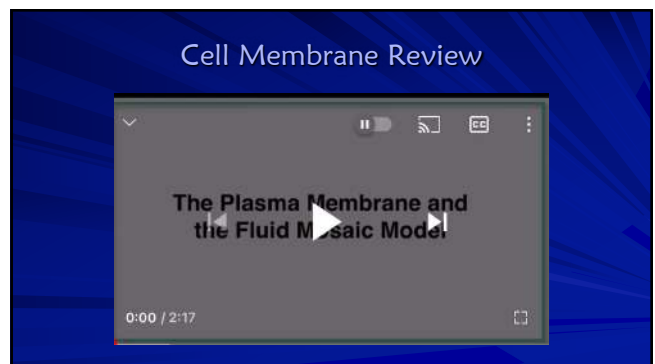
- ### What to Look in a Company
- "Medical grade CBD"
  - Certificate of Analysis (COA) – ask questions
    - Lot specific, comprehensive, is the lab iso-certified for cannabinoids
    - Checking heavy metals
    - Checking for molds, fungus, and bacteria
    - Manufacturing process
    - Planting process
      - Indoor or outdoor
      - Using pesticides
  - The spectrums they have
    - If have isolate – does they do stability testing

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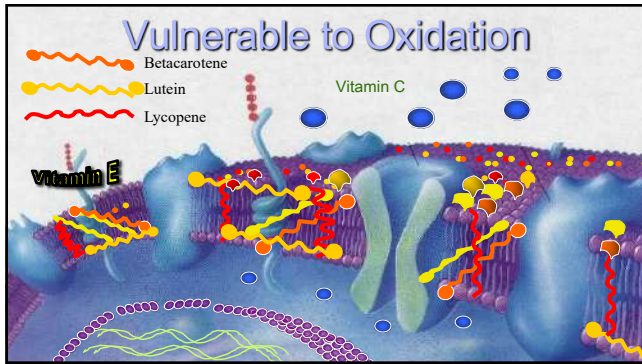
### Inflamm-Aging Metaflammation

Dry Eye, Glaucoma, Diabetic Retinopathy,  
 AMD...and many more

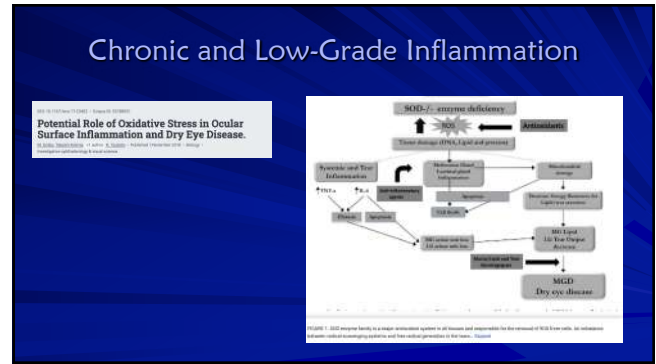
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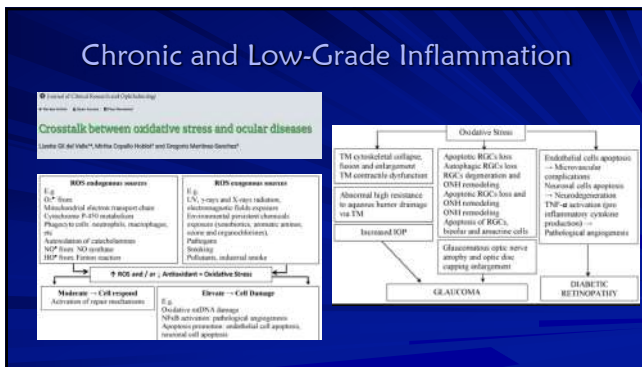
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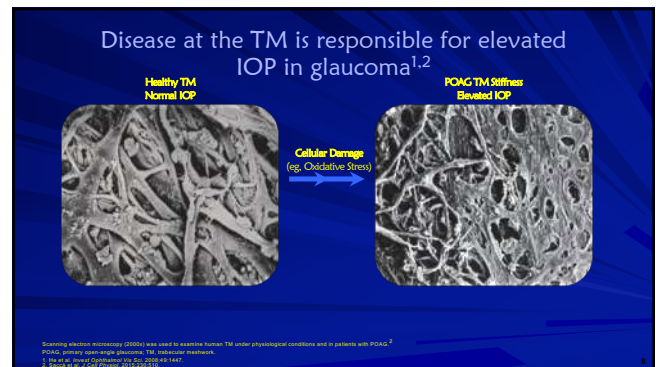
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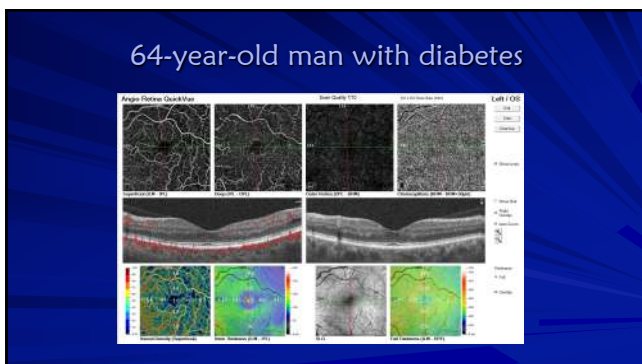
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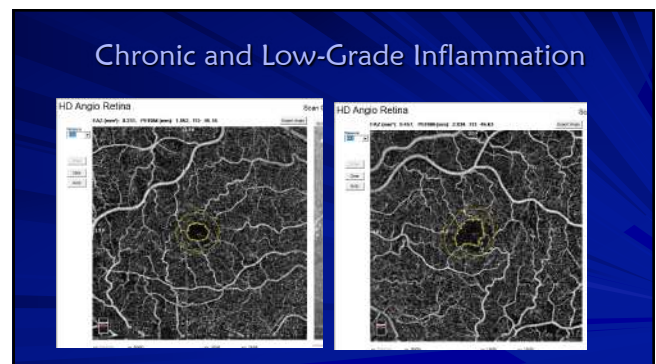
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Investigative Ophthalmology 2019; 58(11):1929-1934  
 doi:10.1093/iov/58.11.1929

**The Diabetes Visual Function Supplement Study (DIVERSS)**

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**FACTORS CONTRIBUTING TO DIABETIC RETINOPATHY**

Ingredient	Amount	% Daily Value
Retene, Stearic Acid, Polyethylene Glycol 400, Polyethylene Glycol 600, Polyethylene Glycol 800, Polyethylene Glycol 1000, Polyethylene Glycol 1500, Polyethylene Glycol 2000, Polyethylene Glycol 3000, Polyethylene Glycol 4000, Polyethylene Glycol 6000, Polyethylene Glycol 8000, Polyethylene Glycol 10000, Polyethylene Glycol 15000, Polyethylene Glycol 20000, Polyethylene Glycol 30000, Polyethylene Glycol 40000, Polyethylene Glycol 60000, Polyethylene Glycol 80000, Polyethylene Glycol 100000	100 mg	20%
...	...	...
Calcium Ion Calcium Carbonate, Di Calcium Malate, Calcium Ascorbate	100 mg	20%

Download figure

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**Ingredients**

Ingredient	Amount	% Daily Value
Retene, Stearic Acid, Polyethylene Glycol 400, Polyethylene Glycol 600, Polyethylene Glycol 800, Polyethylene Glycol 1000, Polyethylene Glycol 1500, Polyethylene Glycol 2000, Polyethylene Glycol 3000, Polyethylene Glycol 4000, Polyethylene Glycol 6000, Polyethylene Glycol 8000, Polyethylene Glycol 10000, Polyethylene Glycol 15000, Polyethylene Glycol 20000, Polyethylene Glycol 30000, Polyethylene Glycol 40000, Polyethylene Glycol 60000, Polyethylene Glycol 80000, Polyethylene Glycol 100000	100 mg	20%
...	...	...
Calcium Ion Calcium Carbonate, Di Calcium Malate, Calcium Ascorbate	100 mg	20%

CONTAINS: Poly-Ethyl Glycol, Hydroxy, Hexa, Cetyl, Butyl, Stearic, Fatty Acids

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**Chronic and Low-Grade Inflammation**

From Oxidative Stress to Inflammation in the Posterior Ocular Diseases: Diagnosis and Treatment

Figure 1

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The ellipsoid zone (EZ) is considered to be formed mainly by mitochondria within the ellipsoid layer of the outer portion of the inner segments of the photoreceptors. However, it was previously known as the junction between the photoreceptor IS/OS.

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**Progress in Retinal and Eye Research**

Interpretation of OCT and OCTA images from a histological approach: Clinical and experimental implications

Abstract: Optic coherence tomography (OCT) and OCTA have been a tool...

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**AMD is a Disease Process that Starts Below the Surface**

Chronic and Low-Grade Inflammation

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### Function Test in AMD Dark Adaptation

- ~ Measures how long to recover from bright light to darkness
  - \* Rod Intercept line (RI) time
- ~ Functional test that can help overcome the challenges in diagnosing AMD
- ~ Alabama Study on Early Age-Related Degeneration (ALSTAR)
  - \* Able to detect subclinical 3 years before clinically visible
  - \* 325 adults without clinically detectable AMD
- ~ Rod deterioration happens in earliest stages of AMD
  - \* Earlier detection before visual acuity
  - \* Sensitivity 90.6%
  - \* Specificity 90.5%



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### Structure - Oxidative Stress with Your OCT Chronic and Low-Grade Inflammation



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### Structure - Oxidative Stress with Your OCT Chronic and Low-Grade Inflammation



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### Integrative Optometry OCT and OCT Angiography

The Connection Between Function, Structure, and Molecular/Nutritional Changes

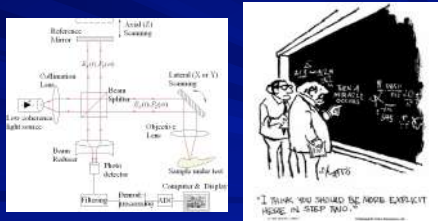
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### OCT and OCT Angiography

Both are Becoming Equally Important in Diagnosis, Management, and Treatment

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### Optical Coherence Tomography Course Design



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### Optical Coherence Tomography

- ~ OCT is an optical signal acquisition and processing method
- ~ Time domain OCT
  - \* 15-16 microns of resolution
  - \* Stratus (Zeiss)
- ~ Spectral domain (SD-OCT) or Fourier domain OCT
  - \* Spatially encoded frequency domain OCT (SEFD-OCT)
  - \* 5-6 microns of resolution
    - Able to see photoreceptor morphology (inner/outer segment)
  - \* 50 times faster than time domain
- ~ Swept source OCT
  - \* Time encoded frequency domain OCT
  - \* 1 micron of resolution
- ~ Future of OCT- intraoperative imaging, blood flow and oxygenation measurements
- ~ May have the possibility to assess retinal pathology like a pathologist

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### OCT Angiography: the Next Chapter in Posterior Imaging

- ~ Images retinal microvasculature without dye injection
- ~ Displays structure and function from a single imaging system

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### Where is the macula?

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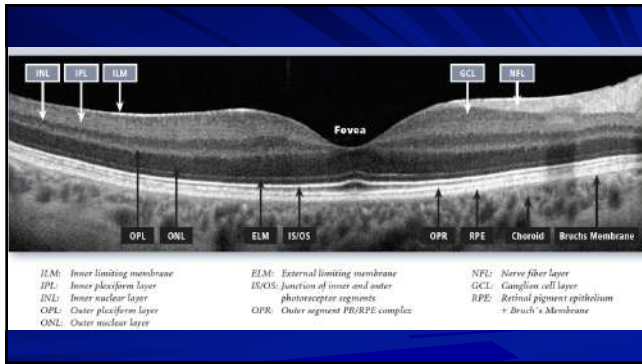
### How large is the macula?

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### 4 Basic Categories: Diseases of the....

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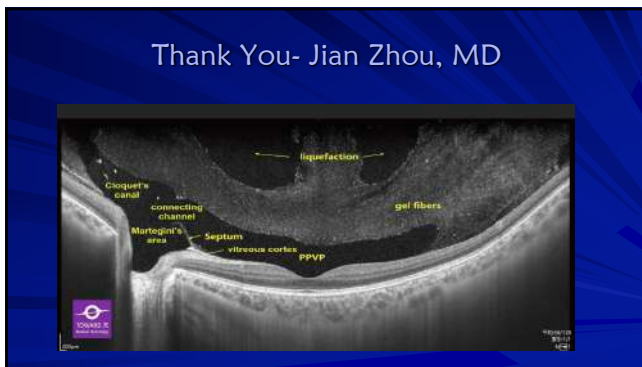
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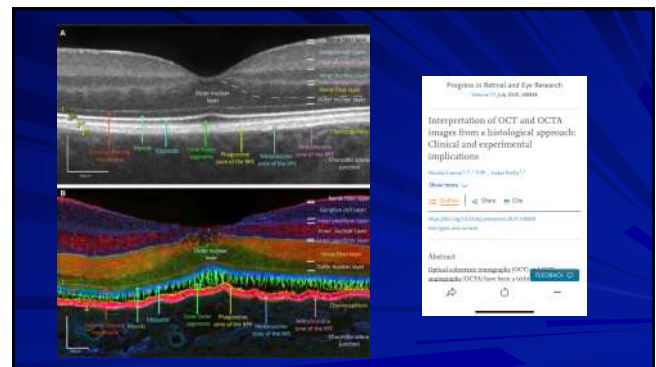
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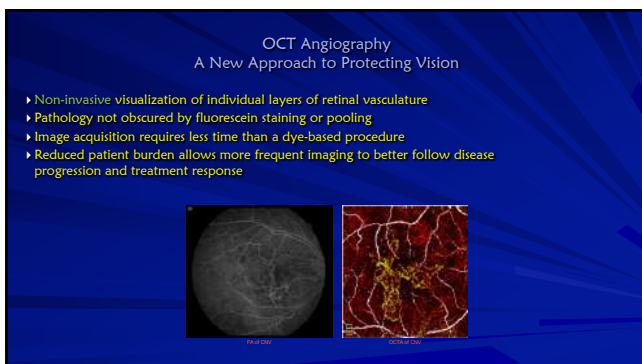
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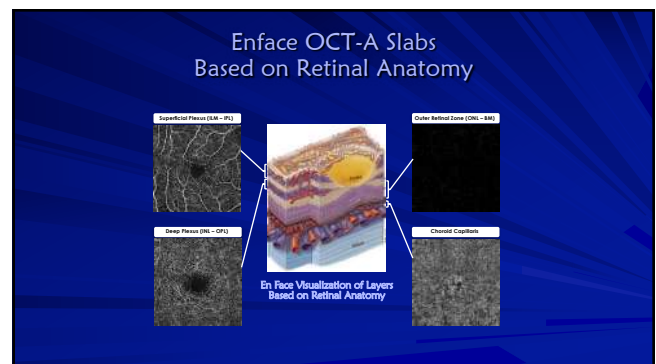
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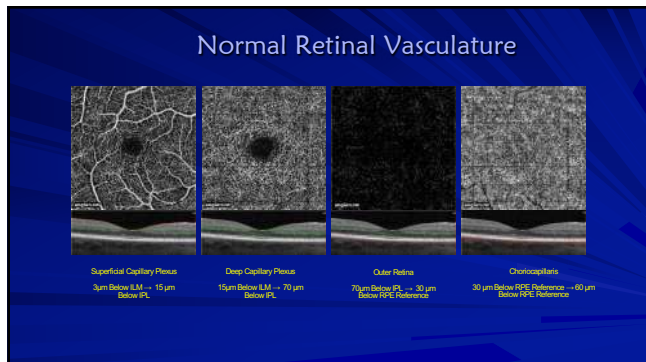
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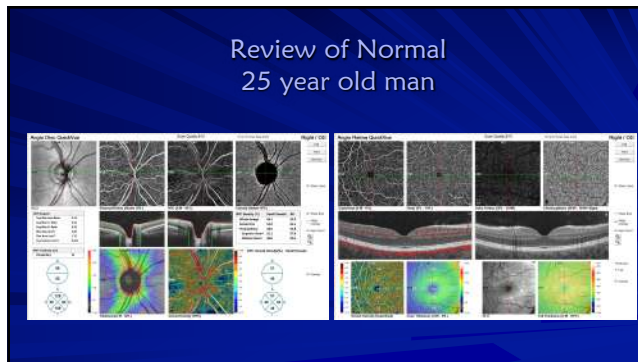
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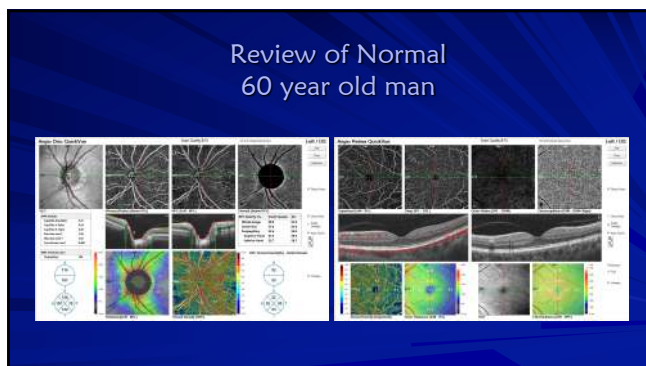
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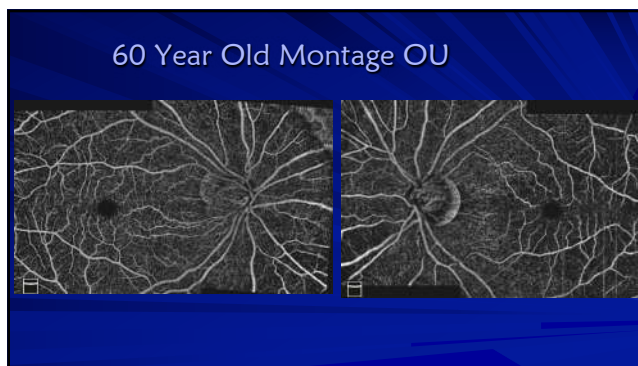
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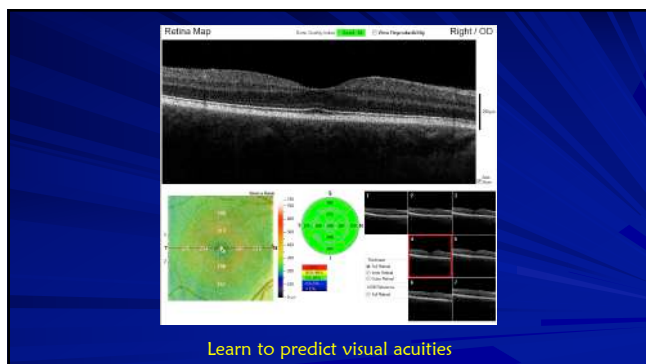
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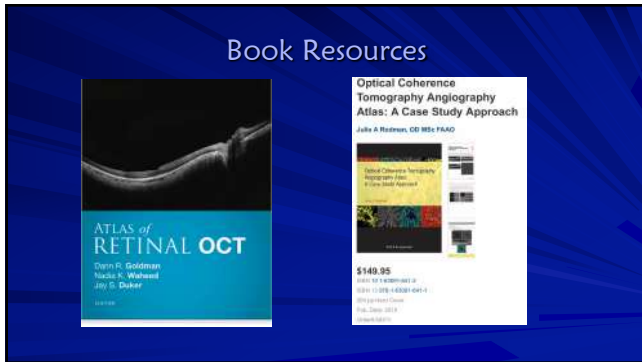


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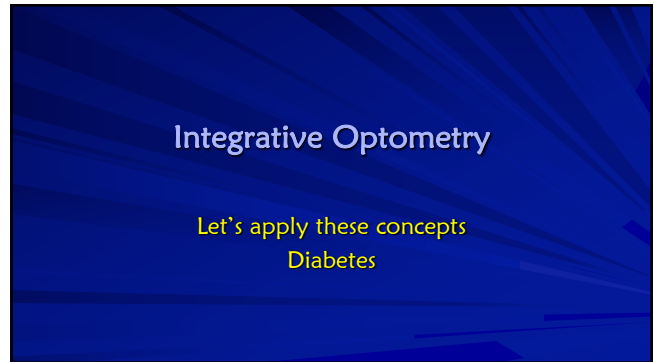


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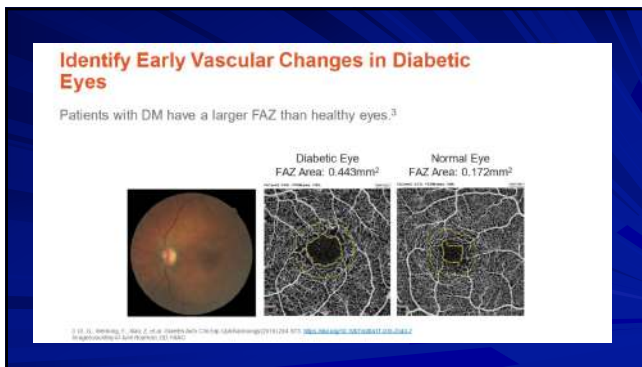




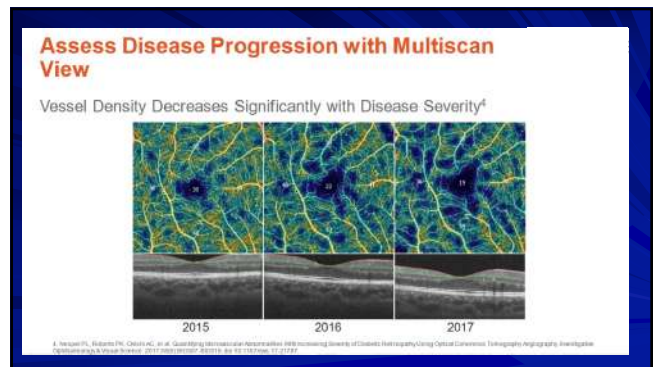
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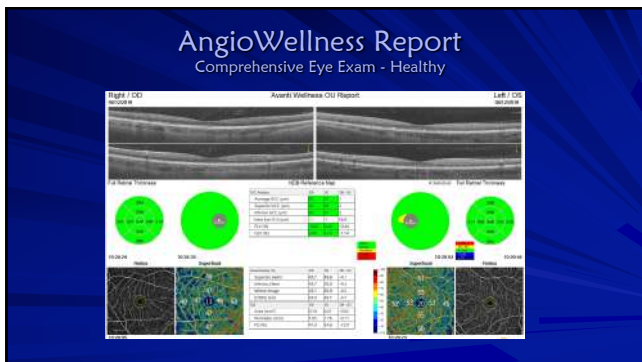
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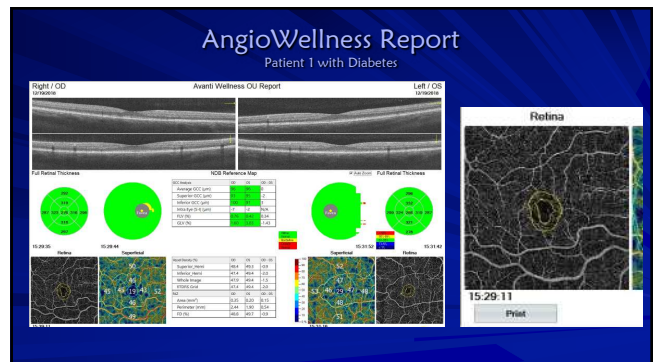
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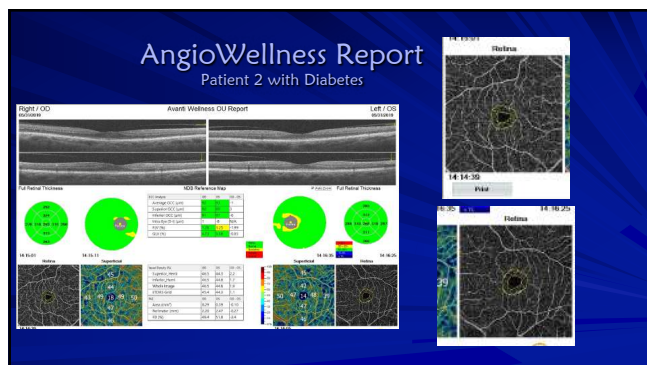
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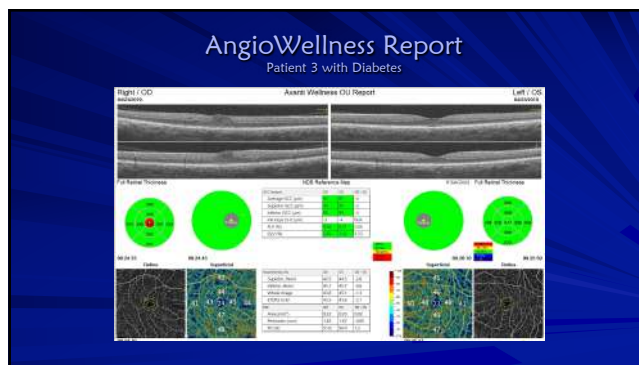
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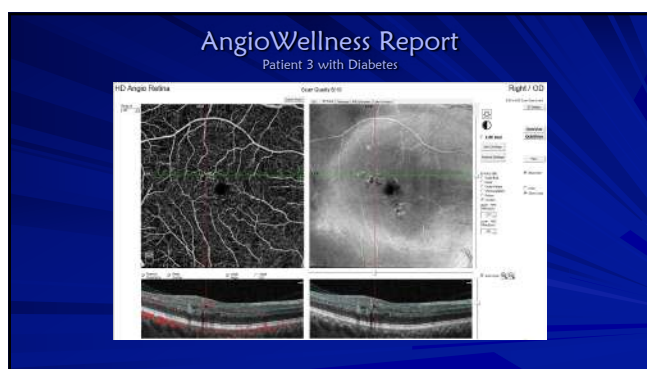
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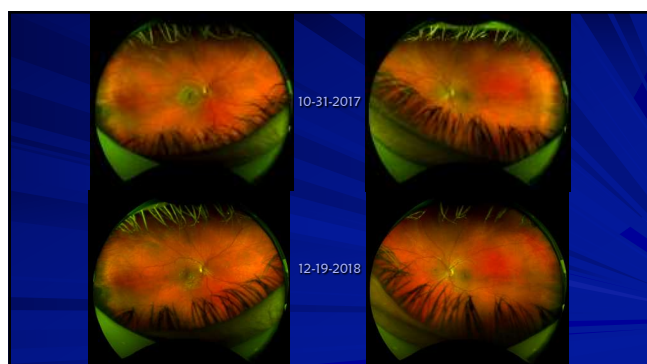


105

29 year old man with diabetes

- ~ Yearly diabetic exam, reports no changes to vision
  - \* Type 1 DM
- ~ BS: 190 this AM, last HbA1c 8.6
- ~ Vision 20/20
- ~ Anterior segment: normal
- ~ Posterior segment:
  - \* Non-proliferative DR
    - Hemes and exudates
  - \* No CSME
- ~ Billed for:
  - \* Exam- 99214
  - \* Optomap, OCT-Wellness, and OCT-A (Angiography)

106



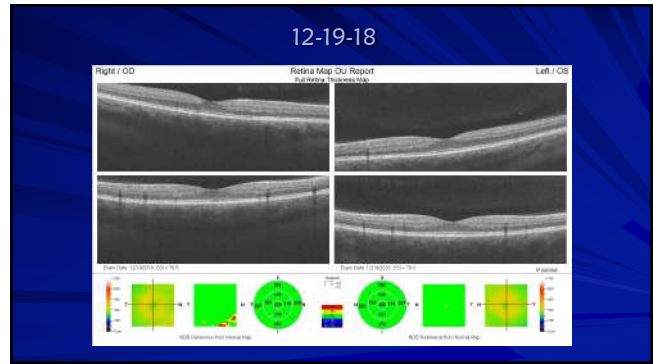
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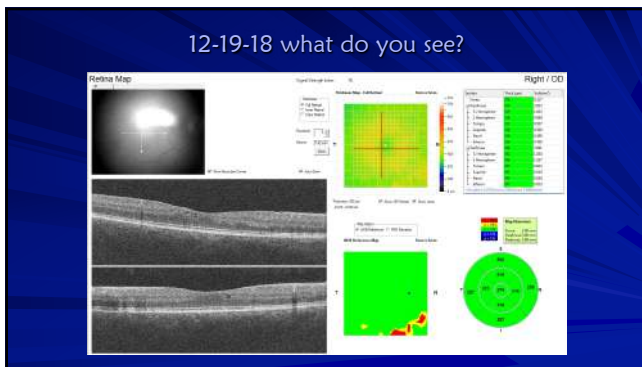
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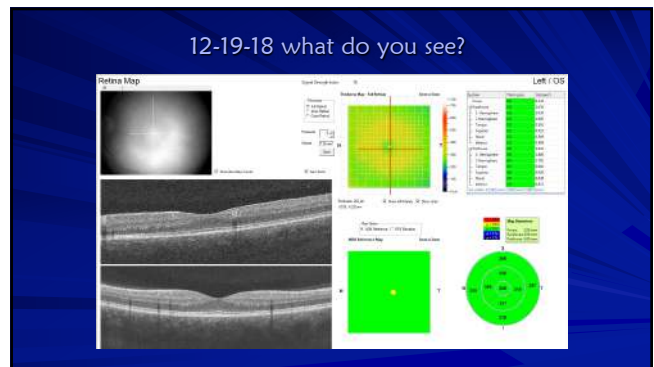
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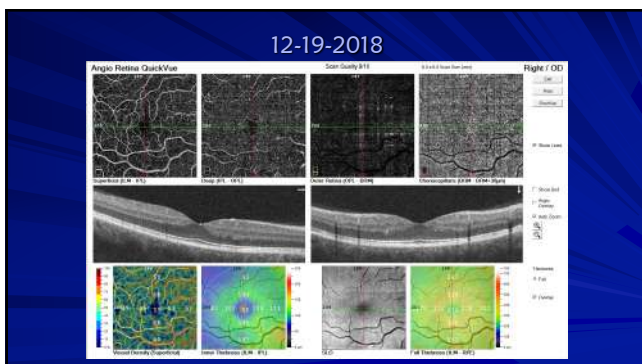
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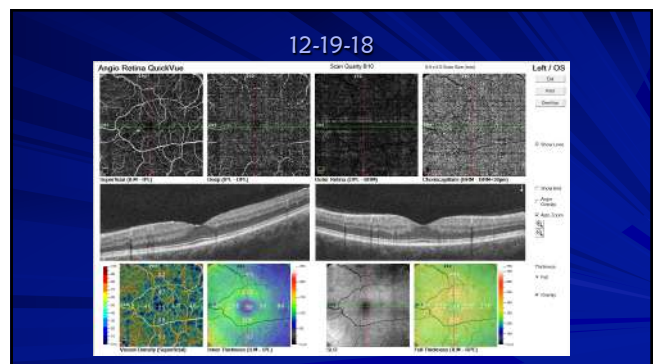
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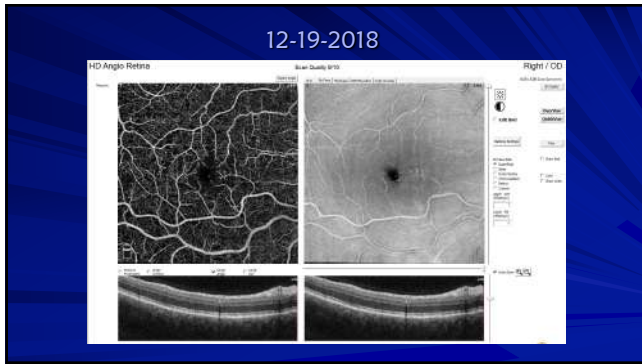
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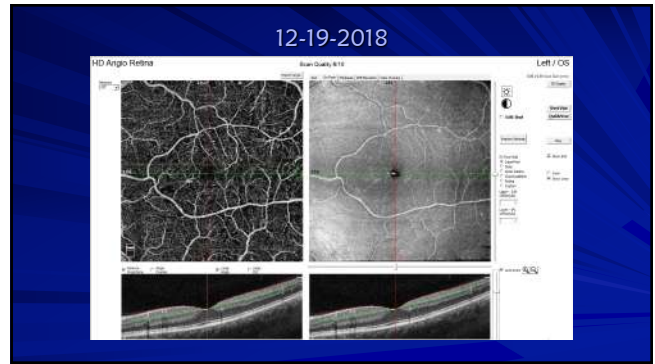
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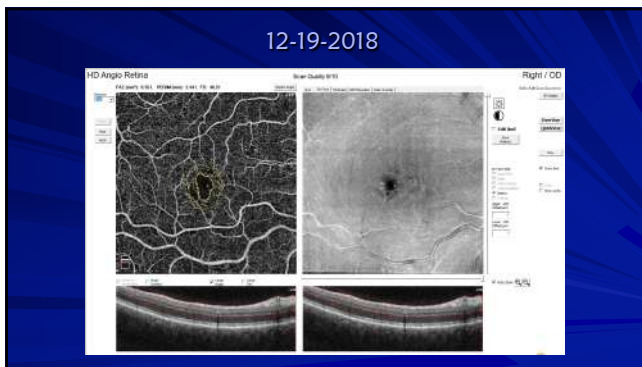
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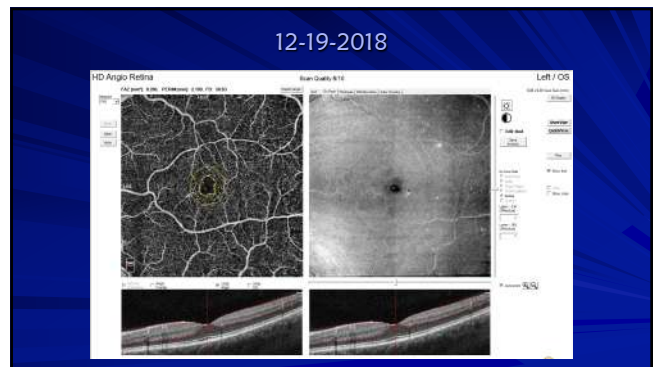
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118

The Diabetes Visual Function Supplement Study (DVFuSS)

PATHWAYS CONTRIBUTING TO DIABETIC RETINOPATHY

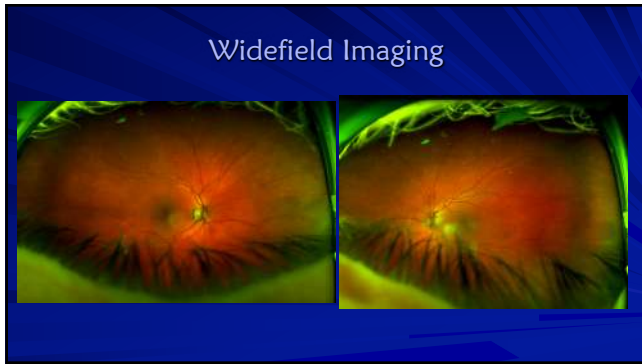
Parameter	Value
Age	58
Sex	Male
Race	White
Diabetes Type	2
Duration	15
HbA1c	8.5
Metformin	Yes
Glyburide	Yes
Invokana	Yes
Vision	20/20
Anterior Segment	Normal

119

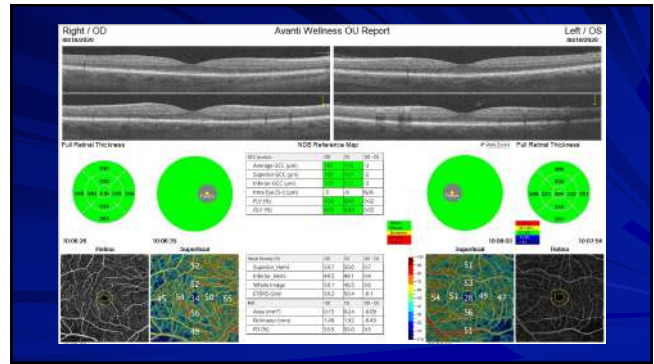
58-year-old man with diabetes

- ~ New patient to the practice
- ~ BS: unsure, last HbA1c unsure
- ~ DM meds: metformin, glyburide, Invokana
- ~ Vision 20/20
- ~ Anterior segment: normal

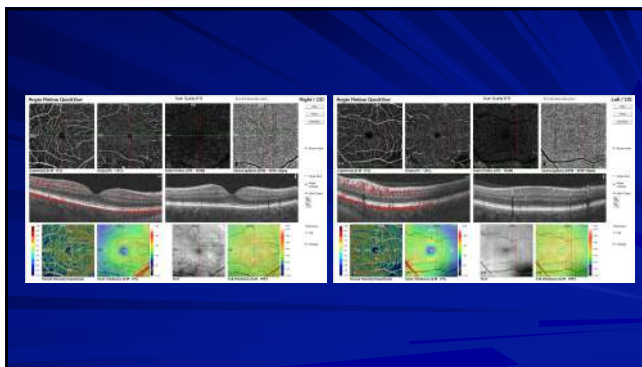
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123

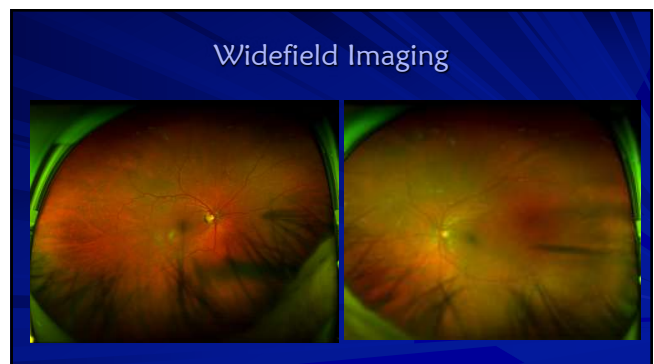


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### 64-year-old man with diabetes

- BS: 134 this AM, last HbA1c 8.0
- DM meds: Novolog and Amaryl
- Vision 20/20
- Anterior segment: normal

125



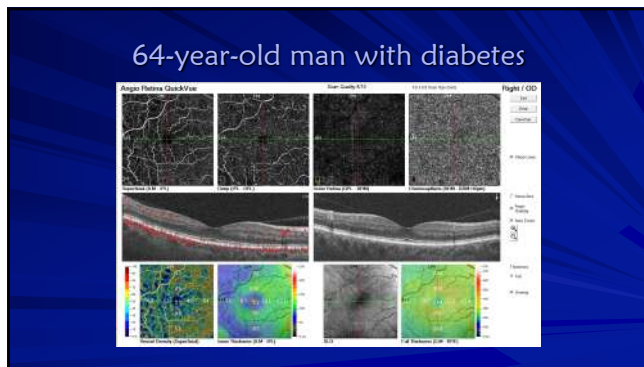
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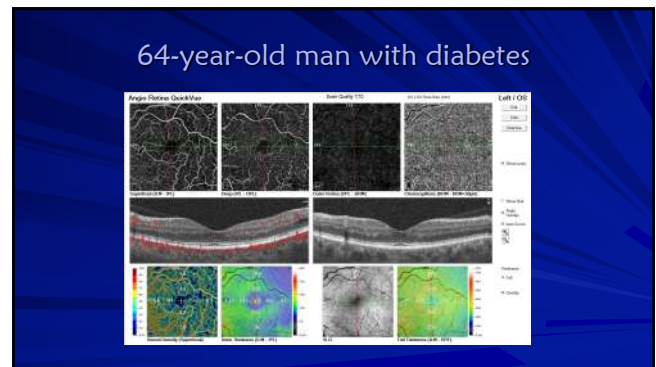
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129



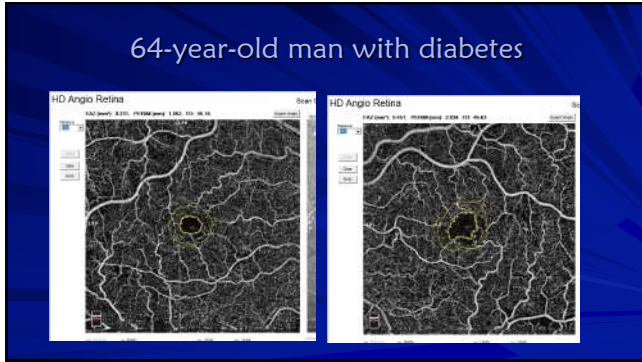
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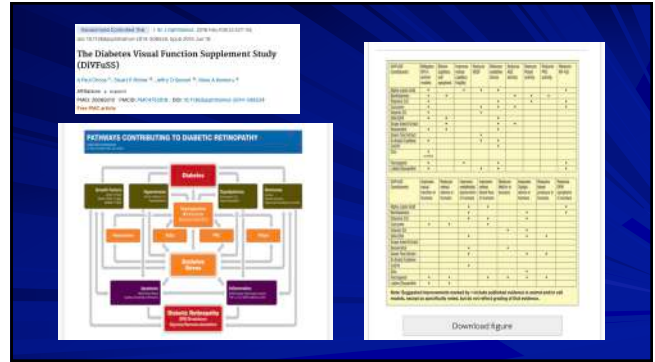
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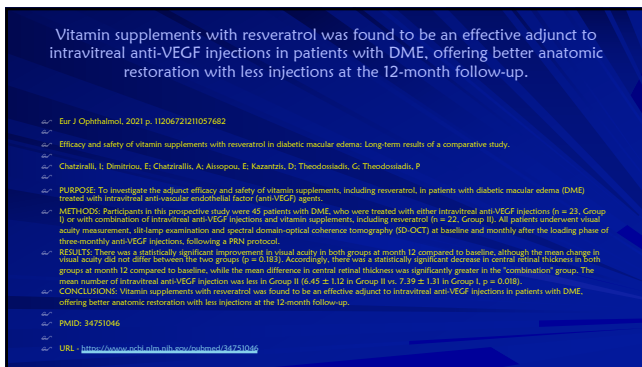
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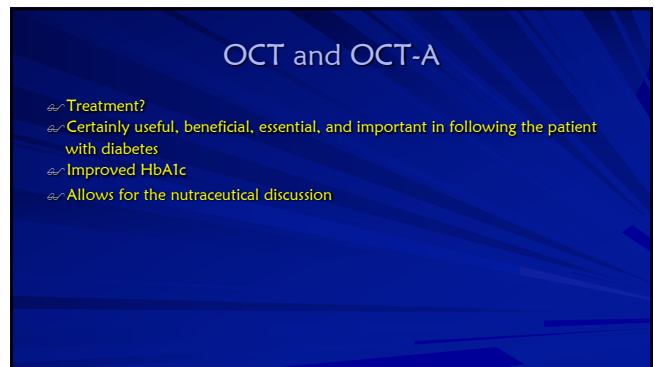
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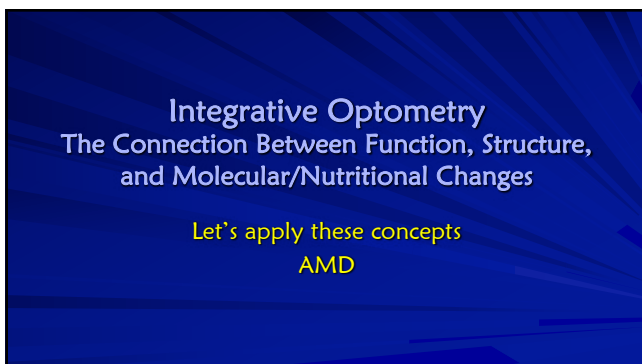
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136



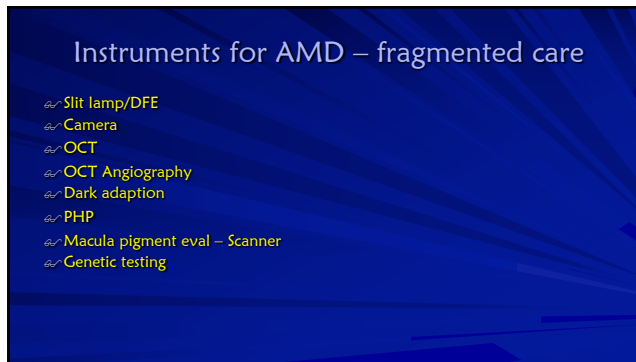
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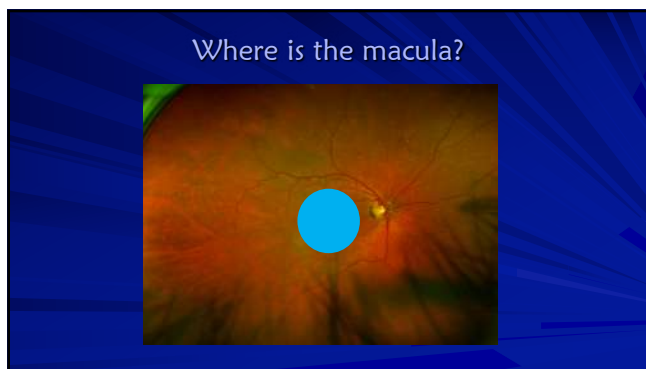
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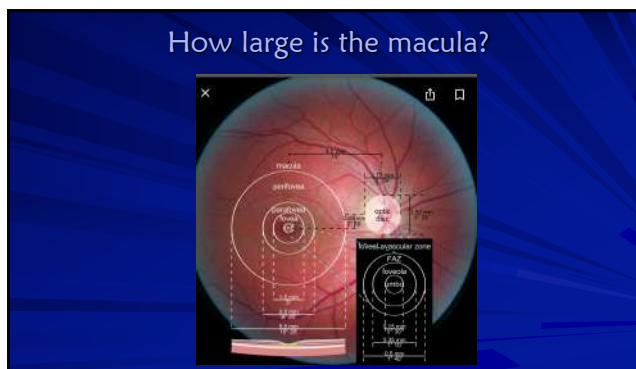
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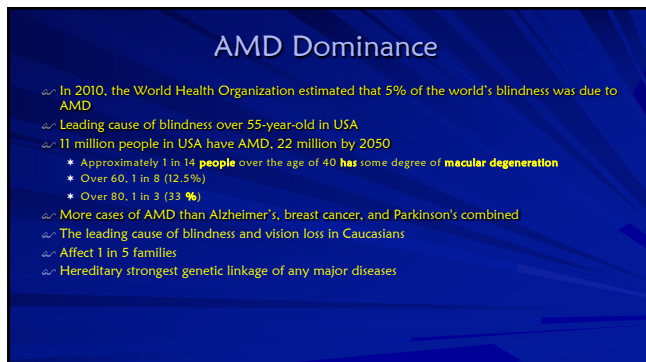
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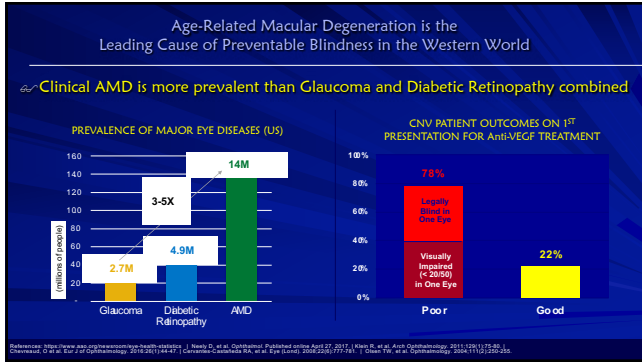


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Primary Eye Care is Missing Visible Disease in 25% of Patients Using Standard Workup

JAMA Ophthalmology | Original Investigation

Prevalence of Undiagnosed Age-Related Macular Degeneration in Primary Eye Care

1288 eyes from 644 people

- Mean age of 69.4
- 36% male

David C. Neely, MD, Kevin J. Bray, MD, Carrie E. Husingh, MPH, Mark E. Clark, BS, Gerald McGwin Jr, PhD, Cynthia Owsley, PhD

**Doctors were aware that they were recruiting patients for an AMD study!!!**

- ✓ 25% consistent with AMD
- ✓ 30% of missed AMD eyes had large drusen (Intermediate AMD)
- ✓ Well-known risk factor for progression to advanced disease
- ✓ ODs and MDs miss AMD diagnosis equally

Reference: Neely DC, Bray JC, Malingro CE, Clark ME, McGwin G, Owsley C. Prevalence of Undiagnosed Age-Related Macular Degeneration in Primary Eye Care. *JAMA Ophthalmol*. 2017;135(6):570-576.

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AMD Considerations and Pearls

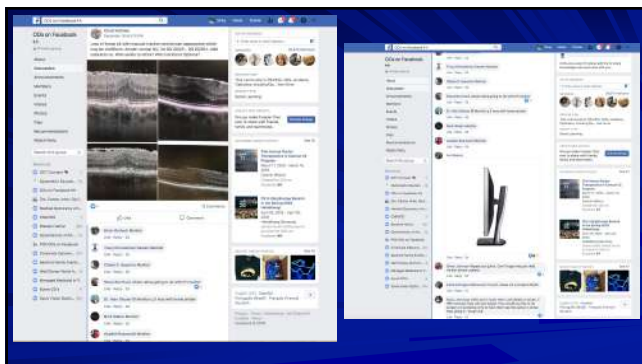
- There is currently no cure for AMD
  - Proper detection and care may prevent significant visual acuity loss in many patients
- Are anti-VEGF injections our patients' best hope?
- Late-stage treatments, albeit necessary, they have little impact on central acuity
  - Impacting our ability to intervene in early to intermediate AMD?

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Optometrists and All Eye Care Professionals Responsibility

- Rethink our responsibility related AMD diagnosis and management
- Commit to that we will do better in
  - Early detection
  - Treatment
- Know, execute, and employ current clinically appropriate Practice Guidelines
  - Those that preserve vision
  - Don't wait until vision has been lost
- Closely monitor and treat the early detected disease
  - If progresses to advanced AMD, better opportunity to save vision

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Early Onset Pathogenesis

- Drusen small or large are not makers for early stage AMD
  - Visible structural evidence of a pathological process
  - Underway for quite some time
- Cholesterol deposits exist beneath the surface long before drusen form
  - Cannot be seen with structure-based methods
  - Cholesterol produced by RPE and deposits into Bruch's membrane
  - Continue to layer in Bruch's membrane
- As this cholesterol accumulates the process unfolds with compromise to the outer retina
  - Inflammation
  - Oxidative stress
  - Disruption of oxygen and nutrients
  - Drusen formation
- Impaired Vitamin A across Bruch's membrane
  - Functional impairment can occur to dark adaptation

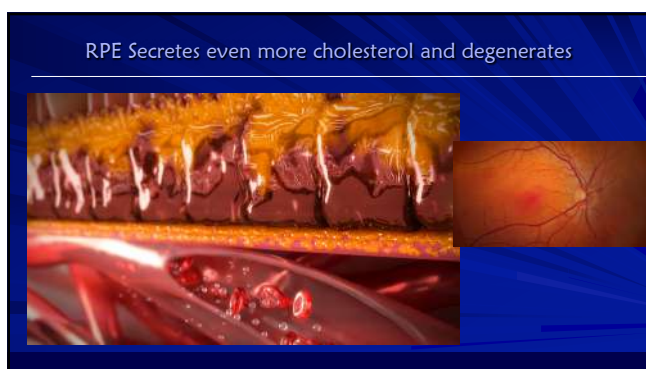
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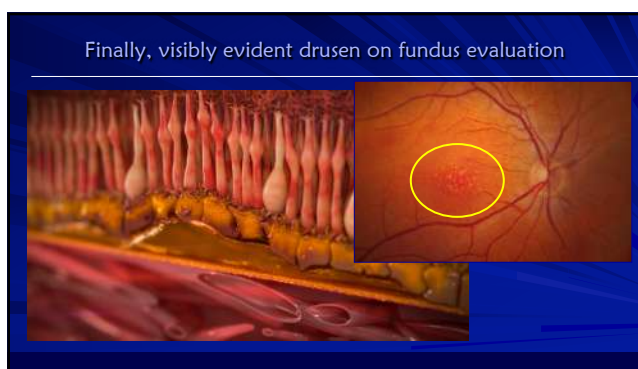
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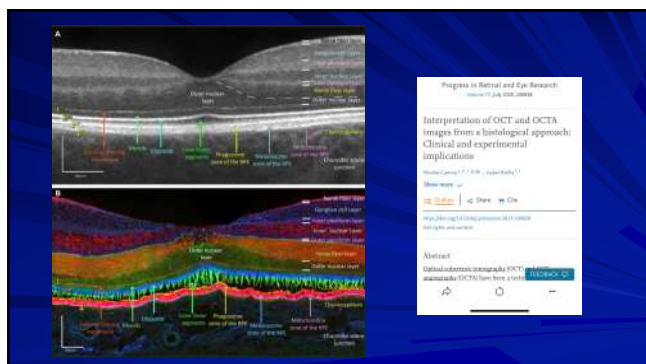
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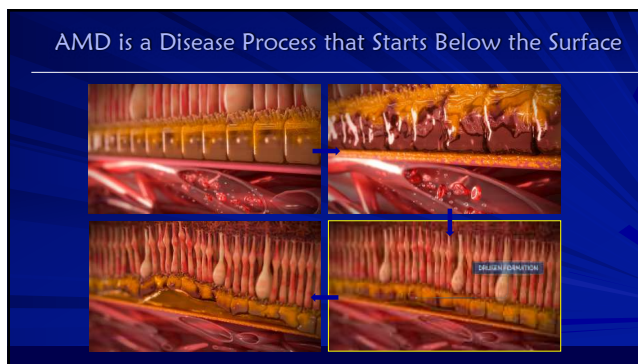
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### Staging of Drusen

What method to detect?

~ Subclinical or sub-structural – cholesterol layer	Functional
~ Small drusen < 63 microns	Exam, photos, SD-OCT
~ Medium drusen > 63 – <125 microns	Exam, photos, SD-OCT
~ Large drusen > 125 microns	Exam, photos, SD-OCT

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### Beckmann Committee Classification of AMD

~ Based on presence of lesions within 2 DD of fovea in either eye

- \* No AMD
  - None or few small drusen, < 63 microns
  - No AMD pigmentary abnormalities
- \* Early AMD
  - Medium drusen, > 63 – <125 microns
  - No AMD pigmentary changes
- \* Intermediate AMD
  - 1 large drusen, > 125 microns
  - Any AMD pigmentary changes
- \* Advanced AMD
  - Any geographic atrophy
  - Choroidal neovascularization (CNV)

158

### Do you see the damage?

159

160

### Oxidative Stress with Your OCT

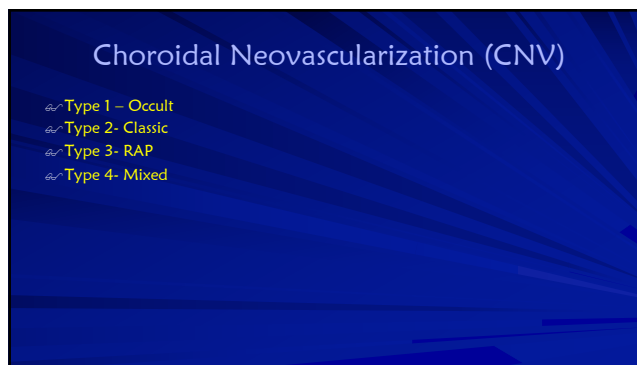
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### Oxidative Stress with Your OCT

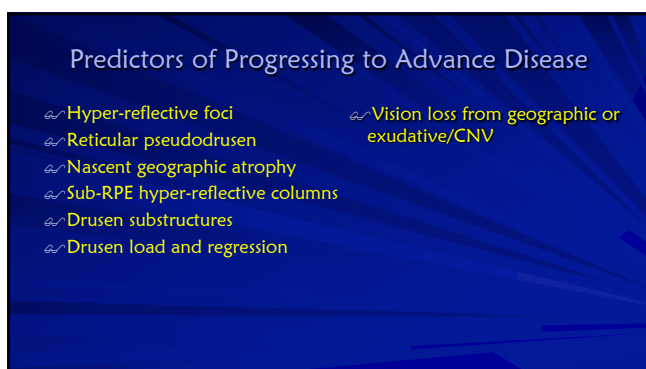
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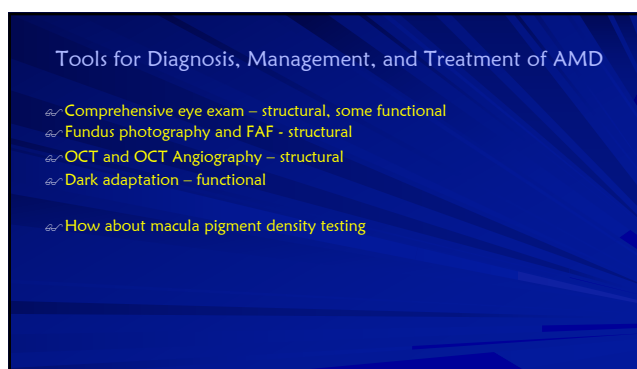
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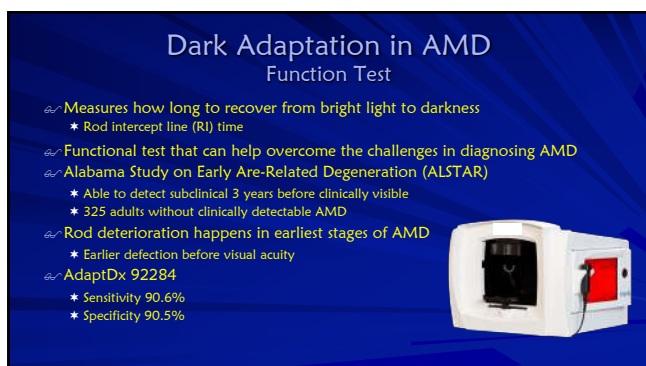
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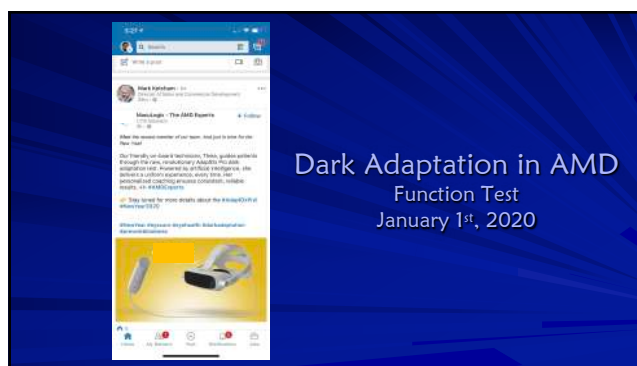
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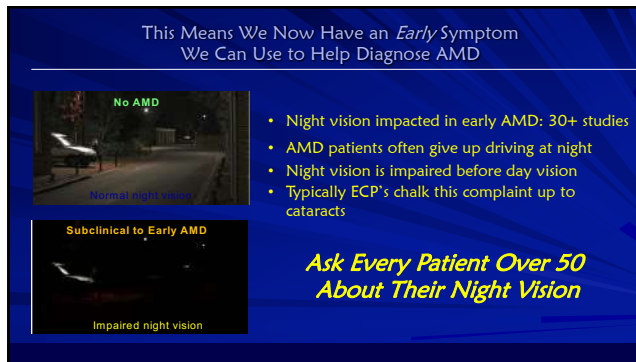
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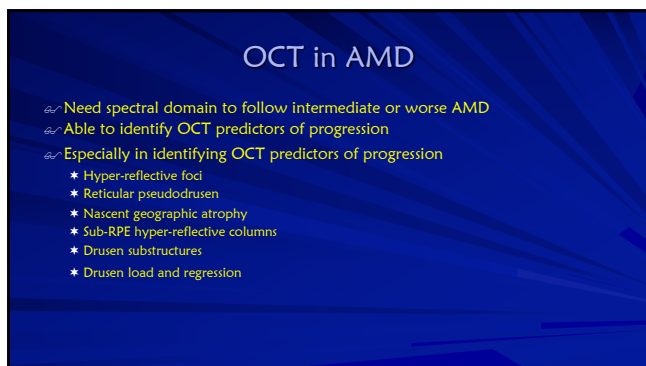
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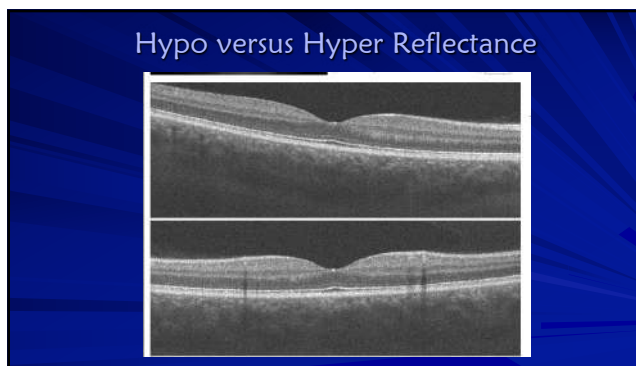
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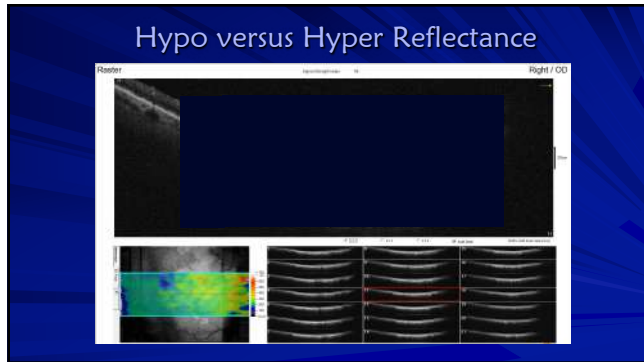
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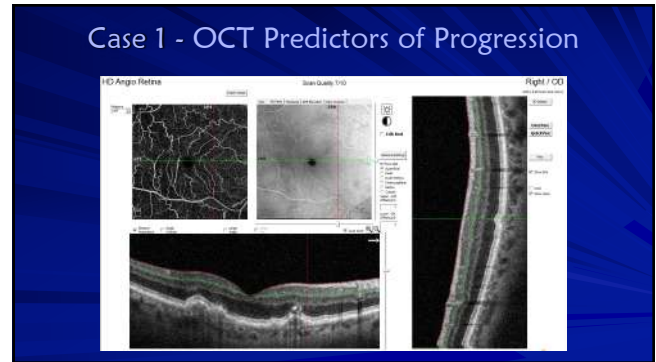
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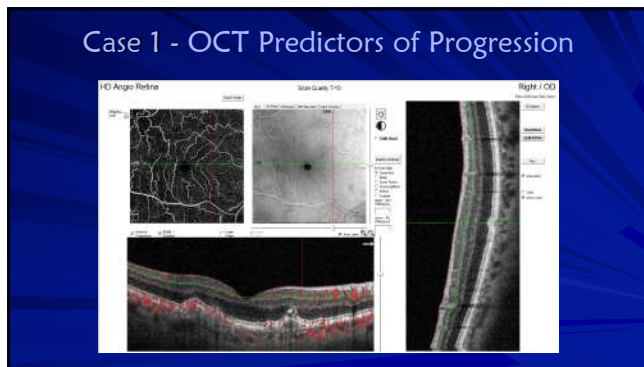
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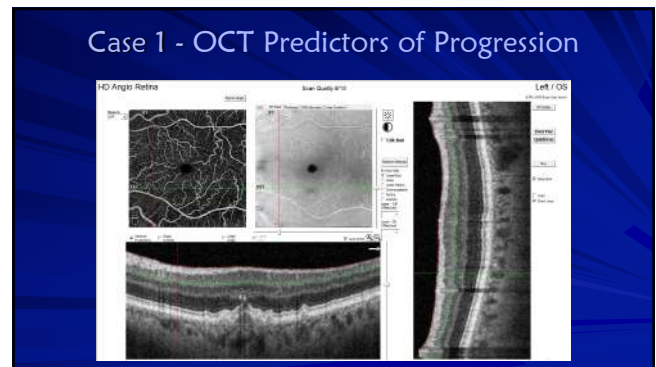
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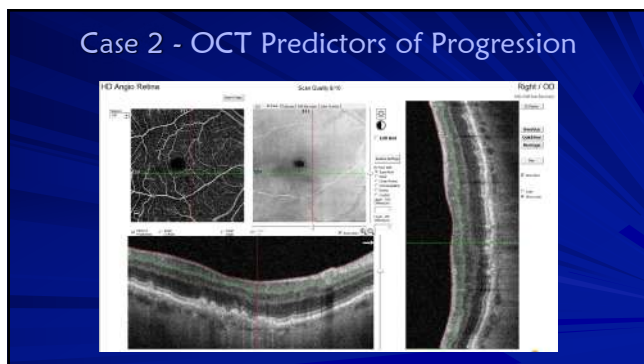
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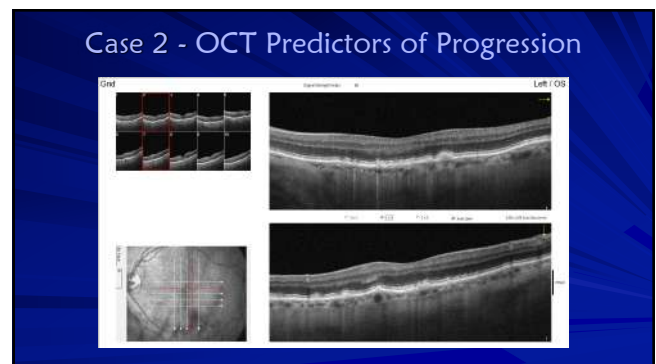
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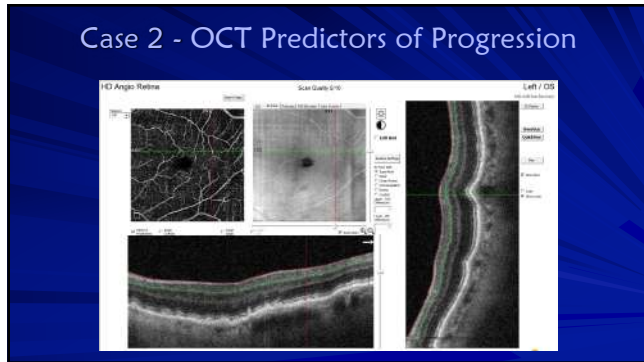
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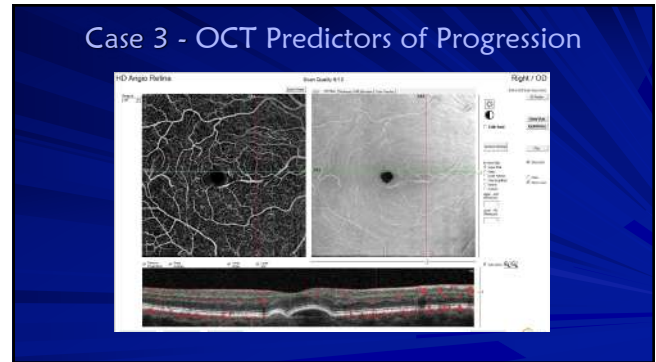
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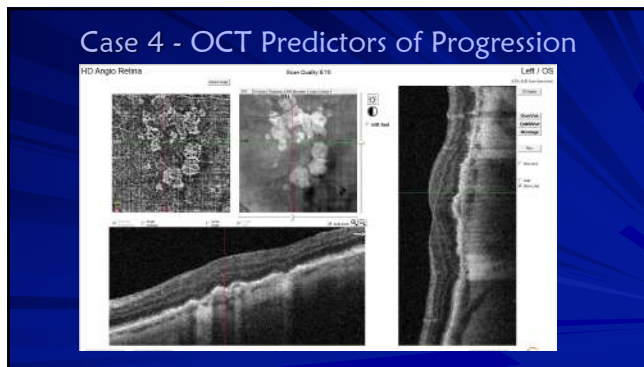
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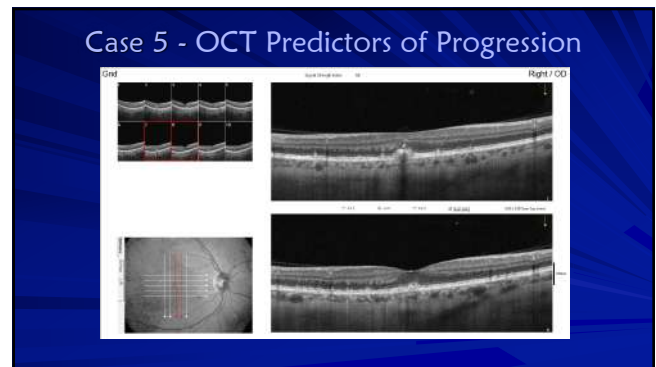
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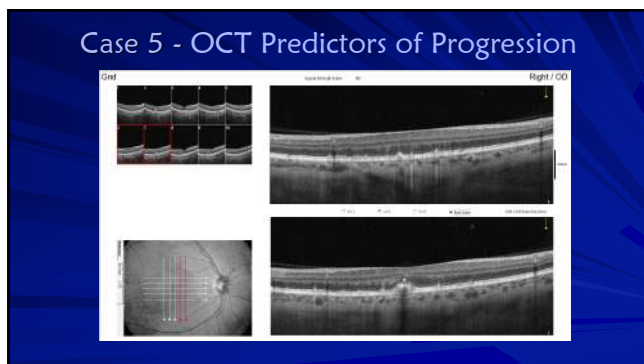
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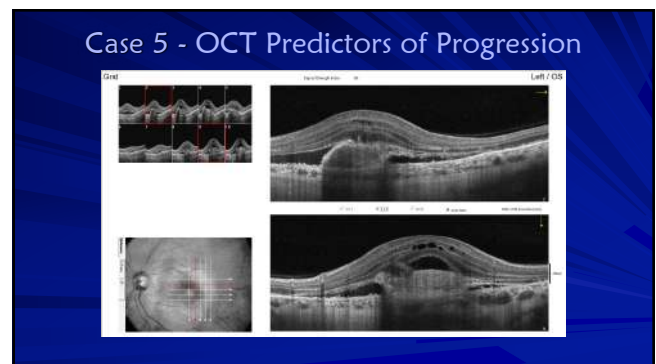
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### OCT Angiography in AMD Structure Test

- ~ Able to identify occult or classic CNV before they leak
- ~ Non-invasive technique
- ~ Subclinical CNV or "Occult non-exudative CNV"
- \* Risk of exudation at 12 months is 15.2 times greater compared to eyes without subclinical CNV

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### Type 1 "Occult" CNV

~ New vessels develop in the choroid  
 ~ New vessels located below RPE and above Bruch's membrane

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### Type 1 "Occult" CNV

- ~ New vessels develop in the choroid
- ~ New vessels located **BELOW RPE** and **ABOVE** Bruch's membrane

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### CNV?

72 y/o Hispanic male  
 20/30  
 History of "Dry AMD"

190

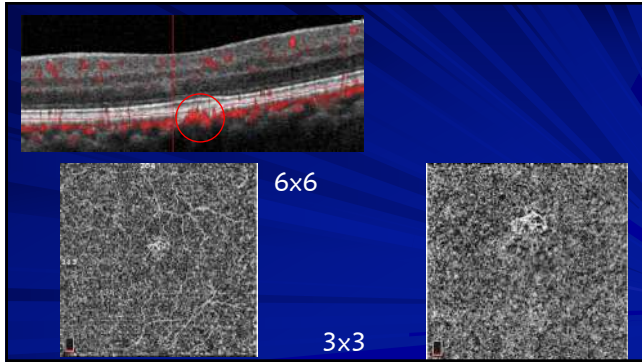
### Multimodal imaging and OCTA

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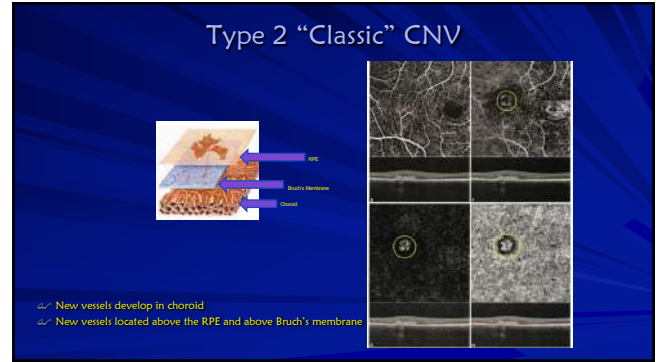
### And the not so obvious ones...

192

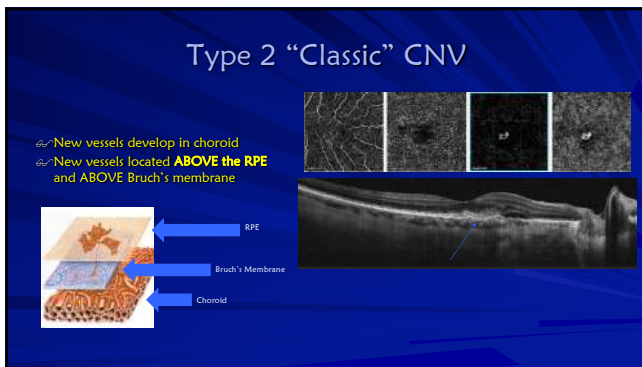




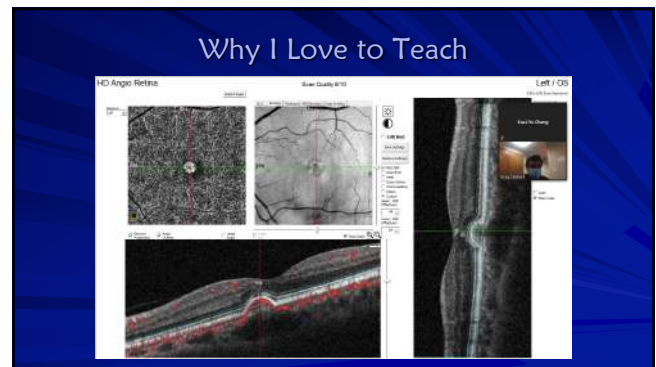
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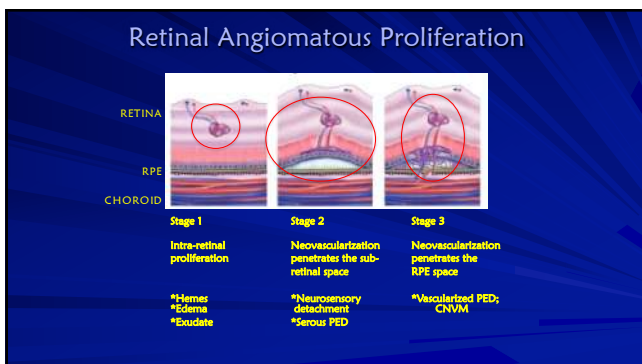
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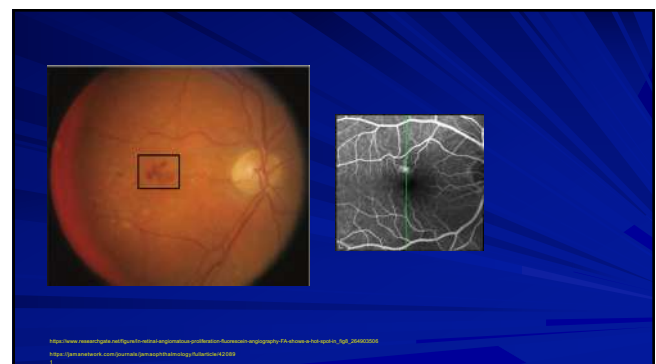
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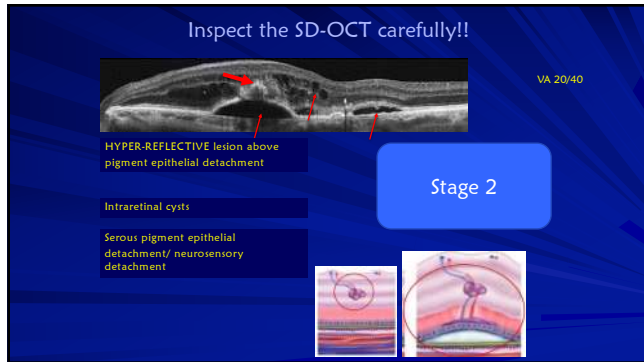
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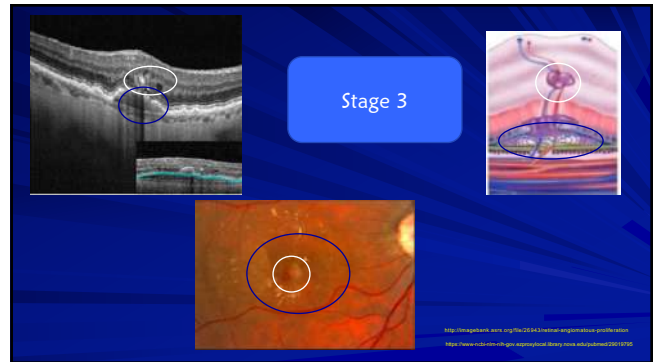
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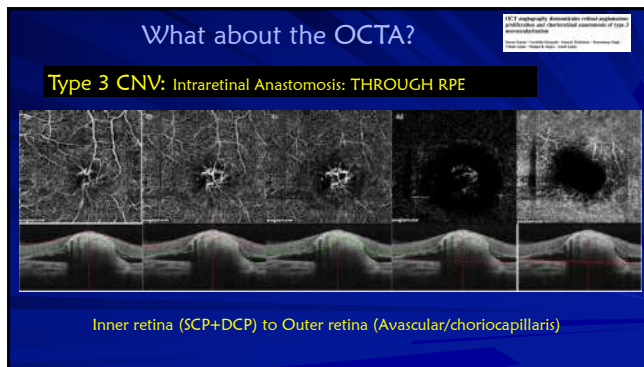
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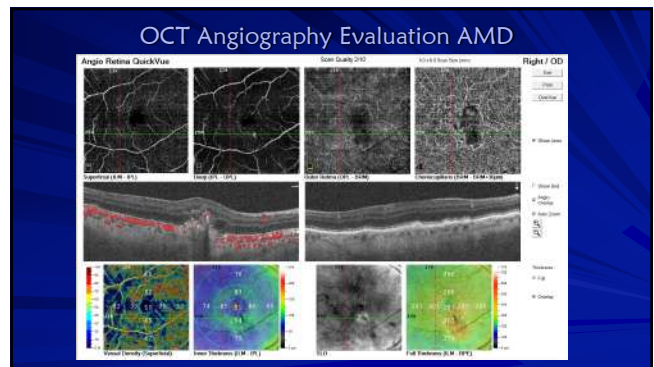
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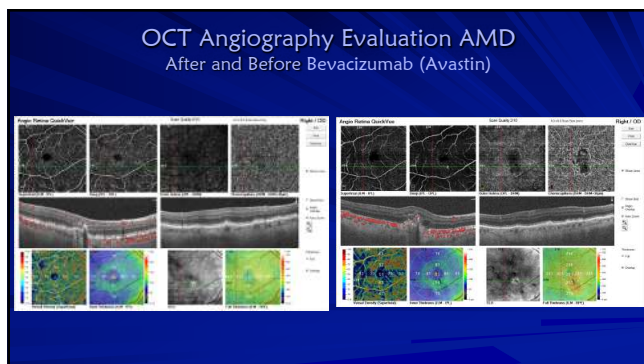
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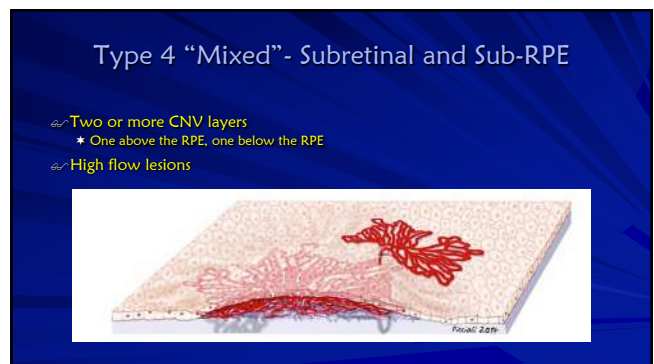
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202



203



204

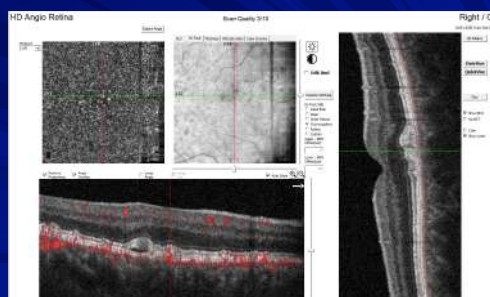
OCT Angiography

Subclinical CNV or "Occult non-exudative CNV"

Risk of exudation at 12 months is 15.2 times greater compared to eyes without subclinical CNV

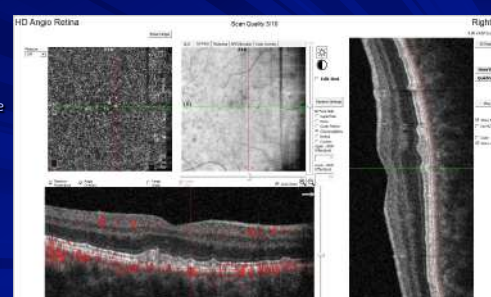
205

Occult Non-Exudative CNV Patient A



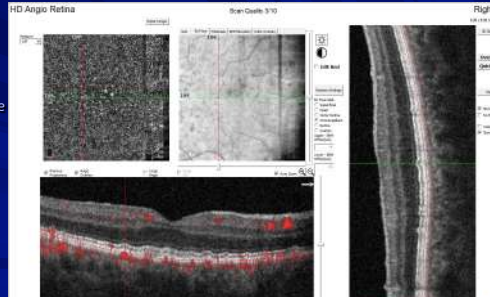
206

Occult Non-Exudative CNV Patient A



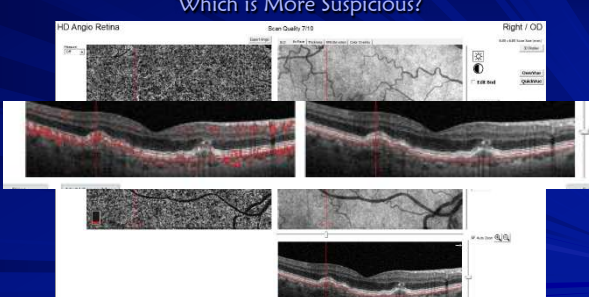
207

Occult Non-Exudative CNV Patient A




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Which is More Suspicious?

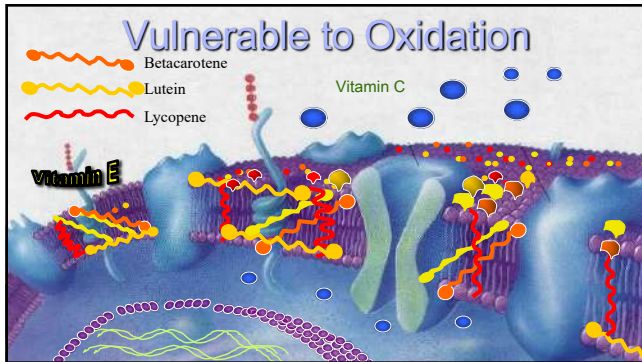


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Molecular/Nutrition



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### Treatments for AMD

~ Early detection and meaningful treatments with significant value, do not cure, but have been shown to slow or halt progression. Not limited to early stages but all stages of AMD

- \* Prescribe smoking cessation programs
  - Smoking and AMD
    - Depletes serum antioxidants
    - Decreases pigmentary density
    - Increases risk to advanced AMD
- \* Lifestyle changes
  - Diet
  - Exercise
- \* Systemic disease management
  - Cardiovascular disease, DM, obesity, high cholesterol

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### Treatment for AMD

~ Nutritional supplements

- \* Sub-clinical/sub-structural or early disease
  - Controversy flourishes
    - No definitive guideline exists
    - Despite consensus evidence suggests using supplements
- \* Intermediate - advance disease
  - No controversy on advocating for supplements
- \* AREDS 1
  - Contains Beta-carotene and no lutein or zeaxanthin, no longer recommended
  - Investigated early AMD, no statistically significant benefit
- \* AREDS 2
  - Recommended for intermediate and advanced AMD, study protocol
- \* The Practical Guide for the Treatment of AMD - 3 primary options
  - Macular pigment supplement
    - Carotenoids: lutein, zeaxanthin, meso-zeaxanthin
  - Carotenoids, antioxidants, zinc, and vitamins C & E
    - AREDS 2
  - Carotenoid macular supplement in subclinical and early AMD. Carotenoid and antioxidant is intermediate and AMD that is progressing

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### Treatment for AMD

~ Retinal light protection

- \* Sun exposure

~ Closer follow up

- \* 12 months is currently accepted as being too long to defect progression
- \* 6 months or sooner based on risk of CNV

~ Low vision and rehabilitation consultation

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### Macular Pigment

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### Macular Pigment

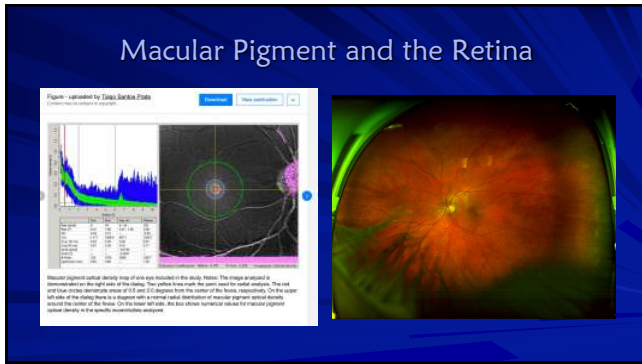
Imaging lutein and zeaxanthin in the human retina with confocal resonance Raman microscopy

Billing LT<sup>1</sup>, Essi M, Truong<sup>1</sup>, Anjaly T, Pagan<sup>1</sup>, Arora D, Bhanuprat<sup>1</sup>, Arundhan Rajagopal<sup>1</sup>, Lu, Yan Chang<sup>1</sup>, Ujjal Sark<sup>1</sup>, Juana M. Prabha<sup>1</sup>, and Paul S. Bernstein<sup>1,2</sup>

<sup>1</sup>Department of Ophthalmology, and <sup>2</sup>Veterans Affairs Eye Center, University of Iowa School of Medicine, Iowa City, IA 52242

Fig. 4. Distribution of total carotenoids in a human macula imaged with CRAM.

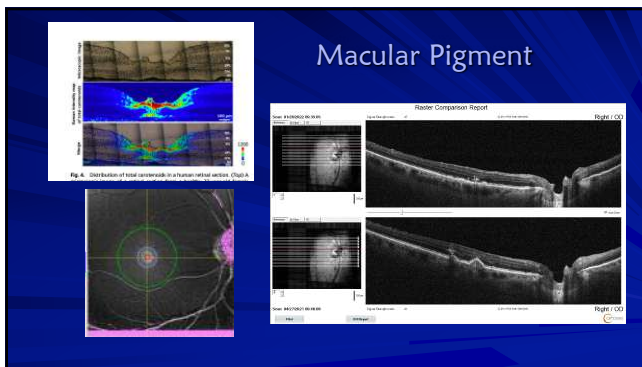
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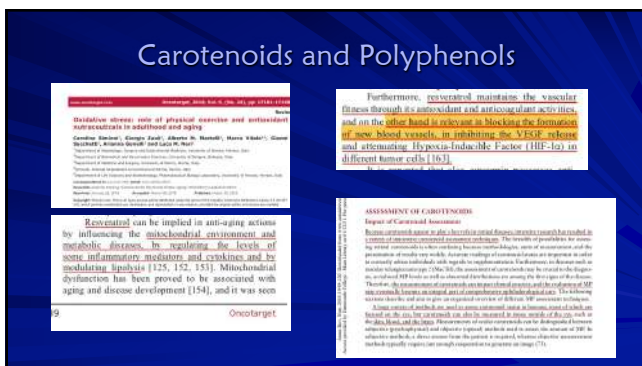
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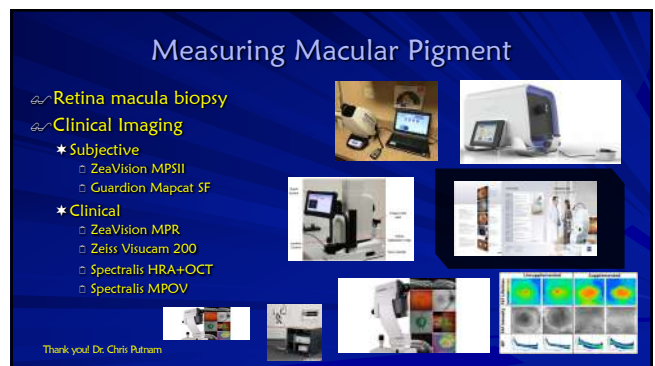
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### Carotenoid (Molecular) Levels

- Quick Test (approx. 30 sec)
- Portable
- Cost Effective
- Remeasure in 60 days
- Reassurance to you and patient


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### Raman Spectroscopy




224

### Chronic and Low-Grade Inflammation



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### Carotenoid (Molecular) Level Validated Numerous Times




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### Measuring Macular Pigment

Biophotonic Scanner


- \* Measures carotenoids
- \* Based on an optical method known as Resonant Raman Spectroscopy (RSS)
  - Used for many years in research laboratories
- \* Skin RSS measurements
  - Noninvasive
  - Objective
  - Reliable methods to assess carotenoid levels
    - Ocular
    - Systemic



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### ARVO STUDY

Interrelationships between Macula, Skin and Serum Carotenoids- Paul Bernstein, Werner Gellerman et al ARVO May 2016



**Conclusions:**  
 "Our results emphasize the importance of measuring the total amount of carotenoids in the macula region using an objective image based modality such as AFI w Spectralis rather than subjective MPD."  
 Skin resonance Raman Spectroscopy of skin carotenoids is a reasonable biomarker of macula carotenoid status, and correlates better than than subjective MPD tests.

The objective, hand scanner is better than the subjective Macuscope, QuantEYE, and Densitometer for estimating macula pigment.



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## Nutraceuticals Molecular

Need to keep it relatively simple

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## Carotenoid Levels

- Quick Test (approx. 30 sec)
- Portable
- Cost Effective
- Remeasure in 60 days
- Reassurance to you and patient

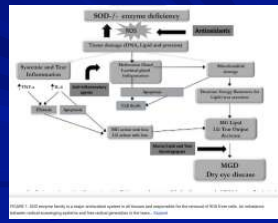
230

## Molecular/Nutrition Quality and Safety



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## Total Eye Coverage Chronic and Low-Grade Inflammation



**Potential Role of Oxidative Stress in Ocular Surface Inflammation and Dry Eye Disease.**

Supplement Facts and Ingredients tables are also visible on the slide.

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## Chronic and Low-Grade Inflammation

Crosstalk between oxidative stress and ocular diseases

**Healthy TM**  
Normal ICP



**POAG TM Stiffness**  
Elevated ICP



Cellular Damage (eg. Oxidative Stress)

Supplement Facts and Ingredients tables are also visible on the slide.

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## Glaucoma

### PERSPECTIVES ON GLAUCOMA

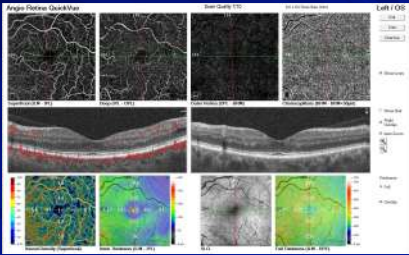
### Antioxidants enhance ocular perfusion in Open Angle Glaucoma

Harris A, et al. Acta Ophthalmol. 2018;doi:10.1111/aos.13530.

"In agreement with previous findings, our results indicate that the supplementation of certain antioxidants may increase blood supply to the orbit and within retinal capillary beds following 4 weeks administration," the authors wrote. "Our data suggest oral antioxidant supplementation may decrease vascular resistance over a longer period of time than previous trials investigated."

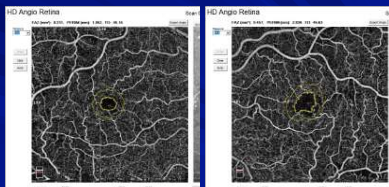
234

### 64-year-old man with diabetes



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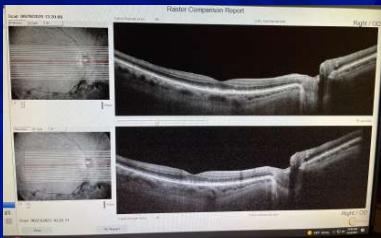
### Chronic and Low-Grade Inflammation



Supplement	Dose	Frequency	Notes
...	...	...	...

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### Chronic and Low-Grade Inflammation

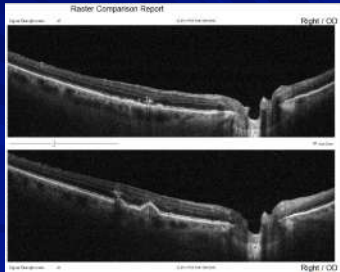


Supplement	Dose	Frequency	Notes
...	...	...	...

Full Retina  
Inner retina - macula pigments  
Outer retina - ellipsoid mitochondria support  
RPE - mitochondria support

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### April 27, 2021 – January 26, 2022 (9 months)




Supplement	Dose	Frequency	Notes
...	...	...	...

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### 53-year-old man

- Family history of AMD
  - Dad with 43 injections for AMD
- Pre-diabetic with borderline HbA1c
- Vision 20/20 OU
- DFE- retina clear
- OCT normal
- Passes dark adaptation



CONGRATULATIONS ON TAKING THE FIRST STEPS  
TOWARDS OPTIMIZING YOUR SCS

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Ingredients	Amount	Daily Dose
...	...	...

Supplement	Dose	Frequency	Notes
...	...	...	...

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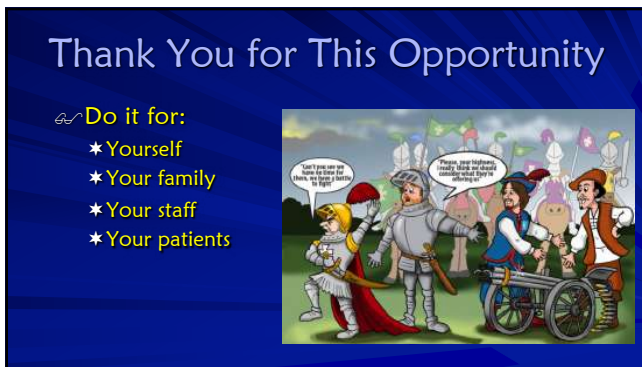




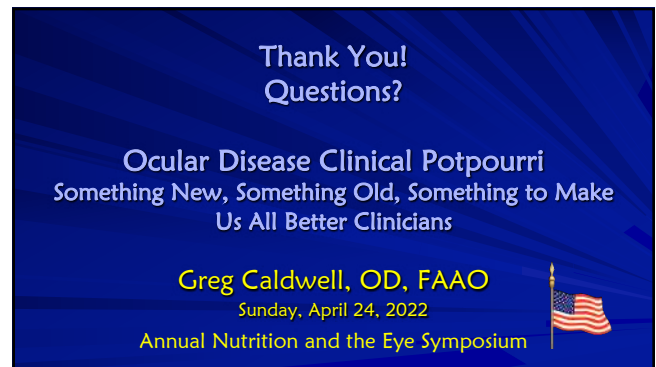
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